NATO ADVANCED RESEARCH WORKSHOP

Current Challenges on Large Supramolecular Assemblies

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Athens, Greece, 31 October - 5 November, 1997

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13. ABSTRACT (Maximum 200 words)

Over the last few years several breakthroughs in the Supramolecualr (SM) domain have being accomplished or foreseen in the near future: bigger molecules are being synthesised; crystals with larger unit cells are being obtained; more and more molecular components are used to build SM compounds with increasing versatility in applications.

This Conference will bring together experts in synthesis and chemical reactivity, in preparation of crystalline compounds, and in methodologies for analysing large SM Assemblies.

The stability and properties of such Assemblies heavily depend upon their three-dimensional (3D) structure involving specific patterns of non covalent bonds and interactions. The difficulty in making complex SM compounds and obtaining structural information has increased to such a level, that a single technique is not sufficient. Various methods are now made available for obtaining, characterising and analysing SM compounds including crystallography, 2D layers, NMR, AFM/STM, FAB/MS, time-resolved phenomena, computational approaches and others. The efficiency of these methods will be examine in the light of recent or foreseen developments in synthesis and formation of large Assemblies. Further improvements can be expected by combining methods that provide complementary information.

14. SUBJECT TERMS

Crystallography and design principles, Synthesis, Reactivity, Molecular Recognition, From 2D to 3D Assemblies, Molecular Recognition and Crystal State, Upgrading Methodologies, Natural and semi-natural systems, Assembly and Self-Assembly

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NATO ADVANCED RESEARCH WORKSHOP

Current Challenges on Large Supramolecular Assemblies
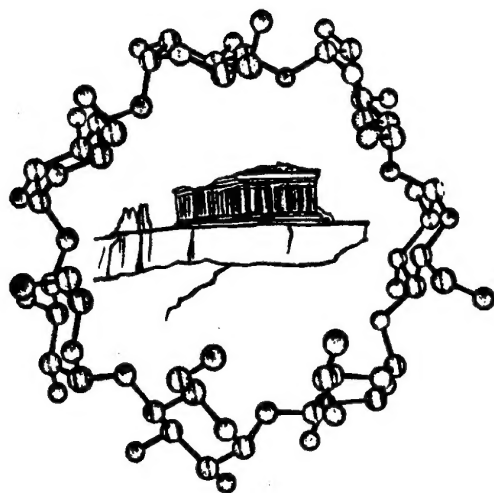
Athens, Greece, 31 October - 5 November, 1997

Ζητεῖ δὴ ἀεὶ τὸ αὑτοῦ ἕκαστος σύμβολον

Συμπόσιον, Πλάτων

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NATO ARW
CURRENT CHALLENGES
ON LARGE SUPRAMOLECULAR ASSEMBLIES

PROGRAMME

a.m. : 8:30 - 12:15
p.m. : 15:00-18:30
DS: Discussion Session comprise talks on late developments, further questions to the speakers and discussion on a specific subject

Fri   31 October
4.00-6.00 p.m.   **Welcome Reception**

6:00-8:00 p.m.   **Crystallography and Design Principles**
                        J. KARLE   J. ATWOOD

Sat   1 November
a.m.   **Synthesis, Reactivity, Molecular Recognition**
                        F. STODDART   N. TURRO
                        D. REINHOUDT A. HAMILTON   DS

p.m.   **From 2D to 3D Assemblies**
                        D. MOEBIUS   M. LAHAV
                        M. ZAWOROTKO   M. WARD   DS

Sun   2 November
a.m.   **Excursion**

p.m   **Molecular Recognition and Crystal State**
                        H. B. BURGI   J. LIPKOWSKI   D. BRAGA
                        G. R. DESIRAJU DS (W. HOSSEINI T. STEINER)

evening   I. KARLE   M. REITER

Mon   3 November
                        Upgrading Methodologies
a.m   G. WIPFF   A. GAVEZZOTTI
                        J. RIPMEESTER A. DORSSELAER
                        DS (C. WEEKS   T. JUNG)

p.m   P. COPPENS   P. RENTZEPIS   DS
                        POSTER SESSION
                        H. GAUB   DS (K. PALEOS)

Tue   4 November
a.m.   **Natural and semi-natural systems**
                        I. KARLE   B. GREEN   W. SAENGER
                        DS (G. TSOUCARIS   I. MAVRIDIS)

p.m.   **Assembly and Self-Assembly**
                        P. ALIVISATOS   J. M. LEHN   DS

Evening   Banquet

KEY SPEAKERS

P. ALIVISATOS Dept. Chemistry, Univ. of Berkeley, USA
Inorganic nanocrystals as building blocks for supramolecular assemblies

J. ATWOOD Chemistry Dept., Univ. Missouri, USA
Spherical molecules and supramolecular assemblies

D. BRAGA Dipt. Chimica G. Ciamician, Univ. Bologna, Italy
Supramolecular Architectures and Hydrogen Bonding in Organometallic Crystals

H.B. BURGI Lab. of Crystallography, Bern, Swizerland
Molecular Recognition of convex fullerene molecules by concave complexing agents.
Structure and Reactivity

P. COPPENS Chemistry Dept. SUNY, Baffalo, NY, USA
Experimental electron densities, their use in the calculation of intermolecular
interactions, and the prospects for the measurement of transient, light-induced changes
in the electron density

G. R. DESIRAJU School of Chemistry, Univ. Hyderabad, India
Use of Non-Conventional Hydrogen Bonds in Supramolecular Synthesis

A. van DORSSELAER LSMBO, Univ. LouisPasteur, Strasburg, France
Can we use mass spectrometry to characterize synthetical and biological supramolecular
assemblies?

GAVEZZOTTI Dipt. Chimica Strutturale & Stereochimica Inorganica, Univ. Milano,
Italy
Self-organization of small organic molecules: crystals, liquids and solutions. Static and
dynamic calculations.

H.E. GAUB Angewandte Physik, Univ. Munchen, Germany
Single molecule force spectroscopy by AFM.

B. GREEN Dept. Pharmaceutical Chemistry, Faculty of Medicine - School of
Pharmacy, Hebrew University, Israel
Esterolytic Catalytic Antibodies - Present Facts and Future Dreams

HAMILTON Dept. Chemistry, Yale Univ., USA
Hydrogen Bonding Motifs for the Formation of Self-Assembled Structures

I. KARLE Naval Research Laboratory, Washington D.C., USA
Crystal Soiving Procedures Applied to Peptide Beta-Foldamers and Channel-Forming
Adamantyl-Peptide Macrocycle

J. KARLE Naval Research Laboratory, Washington D.C., USA
Quantum Crystallography: Features and Applications

M. LAHAV Dept. Materials & Interfaces, Weizmann Inst. Sciense, Israel
Supramolecular Architectures at Interfaces

J.M. LEHN Univ. Louis Pasteur, Strasburg & College de France, Paris, France
Perspectives in Supramolecular Chemistry: From Molecular Recognition towards
Self-Assembly

J. LIPKOWSKI Inst. Phys. Chemistry, Polish Acad. Sciense, Poland

The structure of solvates in the solid state - model systems for heteromolecular association ?

D. MOEBIUS Max-Planck-Inst. fuer Biophysikalische Chemie, Goettingen, Germany
Hydrogen bonds in organized monolayers

D. REINHOUDT Lab. Supramolecular Chemistry & Technology, Univ. Twente,
The Netherlands
Non-covalent synthesis of large supramolecular assemblies

P.M. RENTZEPIS Dept. Chemistry, Univ. California, Irvine, USA
Time resolved diffraction in biological molecules

J. RIPMEESTER Steacie Inst. for Molecular Sciences, Nat. Research Council
of Canada, Canada
Time-resolved studies of clathrate hydrate formation with hyperpolarized xenon.

W. SAENGER Freie Univ. Berlin, Inst. Kristallographie Berlin, & Univ. Erlangen, Inst.
Mikrobiologie Erlangen, Germany
Tetracycline-repressor acts as a molecular switch regulated by tetracyclin binding

F. STODDART Dept Chemistry and Biochemistry, Univ. California, Los Angeles, USA
Synthetic Supramolecular Chemistry

G. TSOUCARIS C.N.R.S. - Univ. Paris-Sud, France
Cyclodextrins: towards bigger Molecules and larger Assemblies

N. TURRO Dept. Chemistry & Chem. Engineering, Columbia Univ., NY, USA
Beyond Supramolecular Chemistry: Supramolecular Aspects of Static and Oscillating
Electric and Magnetic Fields on Chemical Reactivity

M. WARD Dept. Chem. Engineering & Material Sciense, Univ. Minnesota, USA
Crystal Engineering with Two-Dimensional Hydrogen Bonding Networks

G. WIPFF Inst. de Chimie, Strasburg, France
MD simulations on ionophores and ion extraction at liquid-liquid interfaces

M. ZAWOROTKO Dept. Chemistry, St Mary's Univ., Halifax, Canada
Crystal engineering in the context of zeolite and clay analogues: 2-D and 3-D networks
with hydrophobic cavities and channels

ABSTRACTS OF LECTURES

QUANTUM CRYSTALLOGRAPHY: FEATURES AND APPLICATION

J. Karle,[*] L. Huang[*†] and L. Massa[‡]

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Introduction

Quantum crystallography (QCr) is an area of research that arises from the fact that experimental X-ray diffraction data obtained from crystals can also be readily described theoretically by the use of quantum mechanical modeling. The intimate connection between experiment and theory arises from the fact that X-rays are scattered by electrons whose distributions are represented in the experimental data and models of electron density distributions are given by quantum mechanics (Q.M.). An objective of this type of research is to obtain a quantum mechanical model that is consistent with the crystallographic data, thus affording the opportunity to calculate numerous properties of interest, for example, various energies, electron distributions, atomic charges and electrostatic potentials. Our approach to quantum crystallography is based on the use of a single, idempotent density matrix (a projector matrix) [1]. In the initial stages of the process of optimizing the fit of a quantum mechanical model to X-ray diffraction data, it is valuable to have a projector matrix that is as close as possible to the one that results from the fitting process. Such a matrix is obtainable from ab initio calculations. The fitting process involves the adjustment of the values of the elements in the projector matrix and certain other parameters while preserving the idempotency of the matrix and its normalized trace. These properties will be described later on.

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Structures of interest may be too large for <u>ab initio</u> calculations to be made all at once. We have developed a type of fragment calculation in which the individual <u>ab initio</u> fragment calculations can be combined to give a very accurate equivalent to the results that would be made all at once [2]. The fragment calculation scales essentially linearly with complexity. Fragment calculations are, evidently, purely quantum mechanical. The fragment calculations can generate wave functions for rather complex molecules in a free state or in a crystalline environment. The theoretical basis for the fragment calculation may be seen from examination of the theoretical basis for quantum crystallography.

As part of the development of the practical aspects of quantum crystallography, there are special treatments for the experimental data. They concern, for example, the use of Q.M. calculations to remove vibrational effects from the data and a statistical method for detecting and correcting for systematic errors.

QCr proceeds by optimizing the agreement between the structure factor magnitudes from experiment and the structure factor magnitudes obtained from a quantum mechanical model. The only crystallographic information included in the quantum mechanical model concerns the use of atomic positions known from experiment. The fitting process allows for the possibility that the atomic positions may incur some minor adjustments. As noted previously, the Q.M. model has adjustable parameters including those of a projector matrix P that must obey strict conditions, namely,

Idempotency: $P^2 = P$

and Normalization: trace $P = N$

where N is the number of doubly occupied orbitals. These conditions ensure single determinant N-representability. N-representability ensures quantum mechanical validity.

We have presented a general formulation of quantum crystallography which is valid for all 230 space groups, accounting specifically for the symmetry [1]. It can be applied to atomic orbital or symmetry bases. The key features of the presentation concern the quantum mechanical description of an electron density distribution, the definition of a projector matrix which is part of the description and a general expression for the Fourier transform of the electron density distribution that yields the theoretical values for the structure factors. Thus, the theory is in place for making applications of interest. Descriptions of our studies concerning applications of quantum crystallography are being prepared for publication.

Fragment Calculations

In the course of developing the mathematical theory for quantum crystallography, the following equations appeared

$$P = R S$$

$$S = \int \Psi \Psi^\dagger \, dr$$

where P is a projector matrix, a key component of the quantum mechanical model of the electron density, R is a matrix product $C^\dagger C$ where C is a matrix of LCAO coefficients, S is the overlap matrix composed of integrals over all space of products of pairs of orbitals. The use of fragments is based on the fact that the overlap of pairs of orbitals drops off greatly with increase in distance between the orbital centers.

A structure that has been used to test the accuracy of ab initio fragment calculations is leu[1]-zervamicin [2], an antibiotic peptide consisting of 16 amino acid residues. Leu[1]-zervamicin is a membrane active peptide that suggests a model for ion-transport through a membrane with an associated gating mechanism on the

atomic level. With solvent, the structure investigated consisted of 295 atoms, a number that may be currently handled in toto by the ab initio programs offered by Gaussian 94. The combined results of the fragment calculations and the results of the in toto calculation were readily compared. In pursuing the fragment calculation, a set of moieties is selected which, when combined, comprise the entire structure. Nineteen in all were selected for the leu[1]-zervamicin structure, sixteen were based on the 16 amino acid residues and three more were based on the solvent molecules. A fragment consists of two parts, a kernel of atoms and their neighborhood. The neighborhood of a kernel consists of all the atoms that fall within a preassigned distance from the atoms in the kernel. The greater the distance, the greater the potential accuracy. A value of about 5 Å appears to be suitable. Certain adjustments need to be made to the fragments to assure an even number of electrons. This has been achieved by adding hydrogen atoms or additional atoms from the structure that extend beyond the 5 Å limit. The details of this calculation have been described [2]. By calculating difference isodensity surfaces to compare the in toto calculation with the fragment calculation, it was found that the maximum errors, which occurred in only minute volumes, was about 1.2×10^{-3} electrons per cubic angstrom. This calculation involved the use of the simple basis functions, STO3g. The more sophisticated bases should give similar results. With development of programs for ab initio quantum mechanical calculations on parallel computers, it should be readily possible to carry out ab initio calculations for macromolecules by use of fragments.

Nitrocubanes

An ab initio quantum mechanical investigation of a series of nitrocubanes has been carried out preliminary to the application of quantum crystallographic adjustments to optimize the fit of the quantum mechanical models to the experimental data. The molecules of interest consisted of cubane, and the 1,4-dinitro, 1,3,5,7-tetranitro, 1,2,3,4,6,7-hexanitro, 1,2,3,5,6,7-hexanitro, and octanitrocubanes. Three types of quantum mechanical calculations were made to compare with the average C-N and C-C interatomic distances found in crystallographic structure determinations. The 1,2,3,4,6,7-hexanitrocubane and octanitrocubane have not been synthesized and quantum mechanical calculations on them were based on starting structures suggested by those that were known. Evidently, there could be no crystallographically determined structures for them. The purely quantum mechanical calculations involved Hartree-Fock with an STO3g basis, Hartree-Fock with an STO6-31g(d,p) basis and density functional theory with BLYPSTO6-31g(d,p). For the average C-N distances, the Hartree-Fock STO3g calculations were far off, being about 0.05 Å too large, the BLYPSTO6-31g(d,p) calculations were about 0.02 Å too large and the HFSTO6-31g(d,p) calculation were about 0.015 Å too small. For the C-C distances, the STO3g calculations were about 0.01 Å too large, the BLYPSTO6-31g(d,p) calculations ranged from 0.02-0.03 Å too large and the HFSTO6-31g(d,p) ranged from about 0.003 Å too large to 0.009 Å too small. The structures for the theoretical calculations were obtained by determining the atomic coordinates that were consistent with energy optimization for the various models. Although the Hartree-Fock calculation was in best agreement with the experimental values for the interatomic distances, the density functional theory gave lower energies in the energy optimization calculations. Agreement with the interatomic distances may be a useful clue for choosing a

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starting projector matrix for the application of quantum crystallographic adjustments to the experimental structure factor magnitudes.

A number of purely quantum mechanical calculations were made for the various substituted cubanes, based on the results of the energy optimizations. They included the average number of electrons associated with each type of atom present, from which estimates of the charges on the atoms readily follow. Also calculated were total molecular energies, energy differences between molecules with successively increasing nitro substitutions, and energy densities of the crystalline forms of dinitro- and tetranitrocubane. This work is currently being prepared for publication.

Maleic Anhydride

Maleic anhydride has played a valuable role in facilitating our development of the details for carrying out quantum crystallographic calculations.
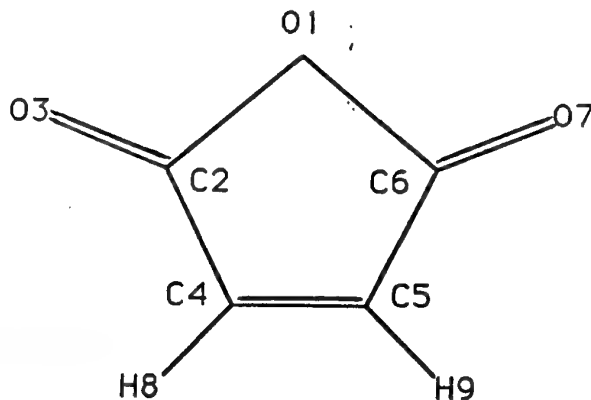
A particularly useful feature is the plane of symmetry that cuts through the molecule in such a way that the charges on both sides of the plane should be equivalent, except, perhaps, for rather minor differences arising from the influences of surrounding molecules. Achieving this in the quantum crystallographic calculations was a valuable learning experience and led to an appreciation of the distinctions

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between various quantum mechanical models, the importance of having high quality experimental data, the need to examine diffraction data for systematic errors and a statistical method for correcting them when they occur.

The optimization of the calculations on maleic anhydride were guided by the measures of agreement of the fit between the experimental structure factor magnitudes and those obtained from the quantum mechanical model. Maleic anhydride crystallizes in space group $P2_12_12_1$ with four molecules in the unit cell. The experimental data included 469 independent structure factor magnitudes which were corrected for thermal and other disorders and also for systematic errors. The quantum mechanical model involved the initial use of the basis, 6-31g(d,p). The quantum crystallographic calculations are characterized by a least-squares procedure for optimizing the fit between the experimental data and the model. As a consequence of these calculations, the standard constants in the Gaussian functions that form the orbitals are, in general, altered, the values of the elements of the projector matrix may change and the x,y,z coordinates also may change. For maleic anhydride, the resulting R-factor as a measure of the agreement between experimental and theoretical structure factor magnitudes was 0.90%.

It should be noted that the end product of quantum crystallographic calculations are static wave functions. The calculations with maleic anhydride indicate that such wave functions can be obtained in good agreement with crystallographic data. They can be used for making a variety of quantum mechanical calculations that concern, for example, various energies and charge distributions. The details of the study of maleic anhydride are being prepared for publication.

References

1. Quantum Crystallography and the Use of Kernel Projector Matrices, L. Massa, L. Huang and J. Karle, International Journal of Quantum Chemistry: Quantum Chemistry Symposium **2 9**, 371-384 (1995).

2. Kernel Projector Matrices for Leu[1]-Zervamicin, L. Huang, L. Massa and J. Karle, International Journal of Quantum Chemistry, Quantum Chemistry Symposium **3 0**, 1691-1700 (1996).

SYNTHETIC SUPRAMOLECULAR CHEMISTRY

Stuart J. Cantrill, Matthew C. T. Fyfe, Frannisco M. Raymo, **J Fraser Stoddart**

Department of Chemistry and BiochemistryUniversity of California at Los AngelesLos Angeles California 90024United States of America

The construction of organic compounds in the laboratory has relied for many decades on the remarkable abilities of the 20th century 'alchemists' — namely, synthetic organic chemists — to make and break covalent bonds. Careful selection of functional groups and reaction conditions, in conjunction with protection/deprotection protocols, constitute the 'secrets' and 'tricks' of their 'magic art' — that of 'traditional' organic synthesis. Indeed, relying on multistep reaction sequences, the total syntheses of extremely complex molecules — *i.e.*, brevetoxin B, palytoxin, and the calichearubicins — have been realized in recent times. These very elegant and successful syntheses have required an enormous intellectual and hands-on effort by large teams of 'alchemists' over rather long periods of time — very often, several years. These remarkable examples, not only illustrate the beauty, but they also represent close to the state-of-the-art, as far as 'traditional' organic synthesis is concerned. Alas, they also highlight the difficulties and the limitations associated with classical organic synthesis. It is the multistep aspect of such syntheses which can be extremely laborious and time-consuming. With the possible exception of some dendritic structures, it is apparent that the construction of nanoscopic structures of the same complexities as those found in biological systems using these classical methods is out of reach, even for the most talented and optimistic of the 20th century 'alchemists'!

Fortunately, the advent of supramolecular chemistry — another form of 'magic art' on an even larger scale — will broaden significantly the number of 'secrets' and 'tricks' available to the 'alchemists' in the 21st century. The use of noncovalent bonding interactions to drive and assist the construction of supermolecules can be exploited at an even higher level of complexity, generating supermolecules, supramolecular arrays, and macroscopic conglomerates with amazing degreees of control and with extremely high efficiencies. In the example illustrated in the figure, a π-electron deficient cyclophane incorporating bipyridinium recognition sites binds a π-electron

rich acyclic guest containing a hydroquinone recognition site, as a result of ′H–′H stacking, [C-H···O] hydrogen bonding, and [C-H···π] interactions. The resulting supermolecule forms a supramolecular array by virtue of strong hydrogen bonding interactions involving the dimeric matching of terminal carboxylic acid groups incorporated at both ends of the guest. Furthermore, π-π stacking interactions are established between adjacent supramolecular arrays, helping to afford ultimately that most robust of macroscopic conglomerates — namely, a crystal. Thus, the process evolves spontaneously form the simple host and guest to the final three-dimensional aggregate without requiring any external intervention — all today's 'alchemist' has to do is to mix the two components in solution and wait for the crystals to appear!

| Primary Structure | Supermolecule | Supramolecular Array | Macroscopic Conglomerate |

INCREASING SUPERSTRUCTURAL COMPLEXITY
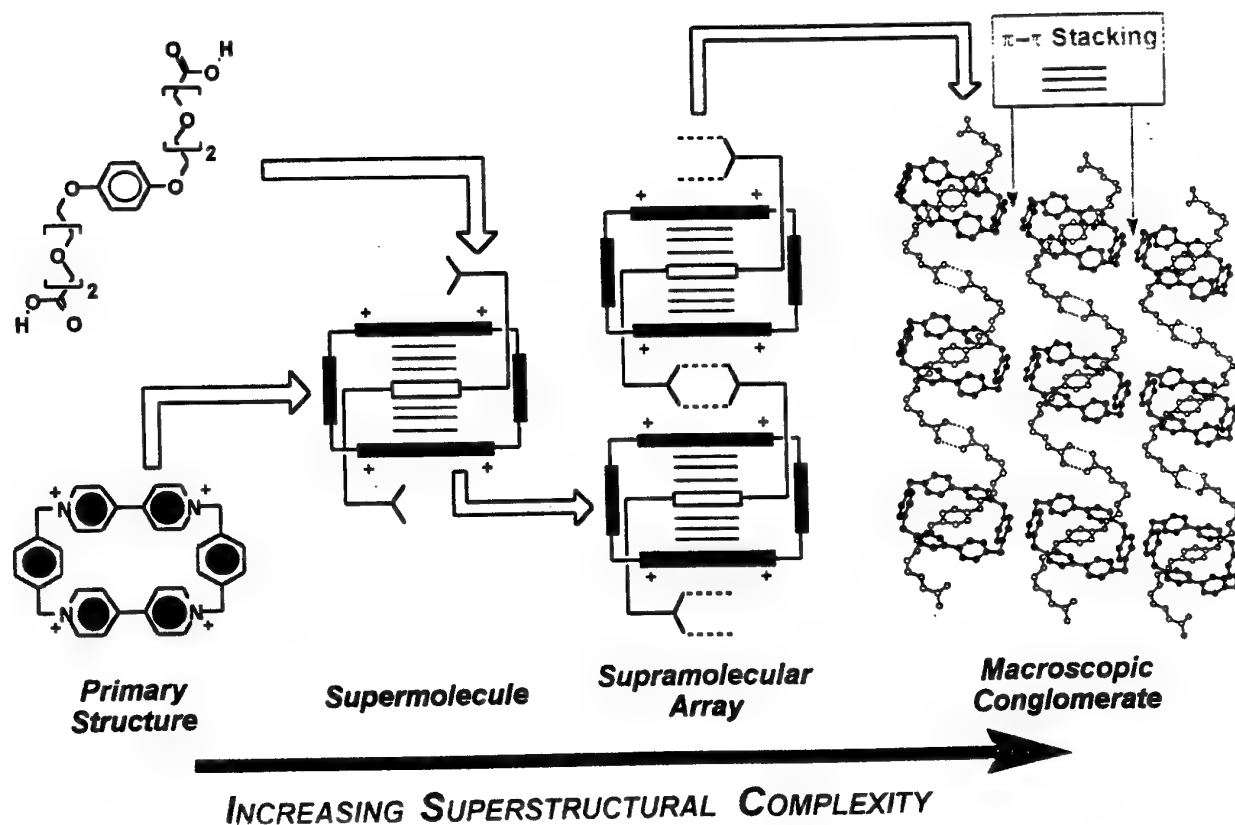
Introduction by design of appropiate recognition sites into simple so-called *supramolecular synthons* has to rely, in large part, on well-established classical synthetic procedures. However, such 'magic' building blocks, once synthesized, possess the information needed to self-assemble spontaneously into a supermolecule which can then again, by virtue of its stereoelectronic

information, grow into a supramolecular array and even a macroscopic conglomerate — *e.g.*, a crystal. Although, the elaboration of such polymolecular systems in solution is still something of a challenge, numerous examples of well-defined, self-assembling systems in the solid state are now known and the previously 'black art' of *crystal engineering* is beginning to become more and more of a respectable and acceptable science.

Two areas of contemporary chemical synthesis have been inspired by supramolecular chemistry: they are (1) the creation of multicomponent supermolecules, supramolecular arrays, and macroscopic conglomerates, utilizing noncovalent bonding interactions, *i.e. supramolecular synthesis*, and (2) the synthesis of discrete molecular entities — held together using covalent and mechanical bonds — aided and abetted by intermolecular noncovalent bonding interactions, *i.e. supramolecular assistance to molecular synthesis*. The impetus for the development of both of these aspects of *synthetic supramolecular chemistry* has been *self-assembly*.

The lecture will focus largely on the first of these areas and show how a number of different recognition motifs (algorithms) can be exploited in an orthogonal fashion, leading to the *noncovalent synthesis* of supermolecules on the one hand and of supramolecular arrays on the other. Employing concurrently such orthogonal recognition algorithms diversifies drammatically the range of self-assembled systems that are accessible to the contemporary supramolecular chemist. They permit the construction of supermolecules and supramolecular arrays that would have been inconceivable not all that long ago. Indeed, the operation of several recognition algorithms simultaneously in supramolecular syntheses may be likened to a 'traditional' synthetic chemist employing several different covalent bond-manipulating reactions, in a synthetic sequence, during the total synthesis of a complex natural product.

Highly Relevant Literature

- For a superb lesson in the 'magic art' we call *Organic Synthesis*, look at:

  Nicolau, K.C.; Sorensen, E.J. *Classics in Total Synthesis*, VCH: Weinheim, 1995.

- For an intellectually stimulating analysis of the 'magic art' he calls *Supramolecular Chemistry*, read:

  Lehn, J.-M. *Supramolecular Chemistry*, VCH: Weinheim, 1995.

- For a thought-provoking discussion of *Crystal Engineering* that takes it beyond being a 'black art', browse through: Desiraju, G.R. Crystal Engineering, Elsevier: Amsterdam, 1989.

- For striking examples of *Noncovalent Synthesis* in action, refer to:

  Whitesides, G.M.; Simanek, E.E.; Mathias J.P.; Seto, C.T.; Chin, D.N.; Mammen, M.; Gordon D.M. *Acc. Chem. Res.* **1995**, *28*, 37–44.

- For an explanation of the concept of *Supramolecular Synthons*, study:

  Desiraju, G.R. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2311–2327.

- For a 'personal' account on *Synthetic Supramolecular Chemistry*, see:

  Fyfe, M.C.T.; Stoddart, J.F. *Acc. Chem. Res.* **1997**, *30*, 393–401.

- For an overview on the realm of *Self-Assembly Processes*, examine:

  Philp, D., Stoddart, J.F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1154–1196.

- For some fascinating examples of *Supramolecular Assistance to Molecular Synthesis*, remember to look out for: Gillard, R.E.; Raymo, F.M.; Stoddart, J.F. *Chem. Eur. J.* In press.

Beyond Supramolecular Chemistry: Supramolecular and Übersupramolecular Aspects of Chemical Structure and Reactivity: Static and Oscillating Electric and Magnetic Fields, Coherence and Cooperativity

N. TURRO

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Introduction

The emerging paradigm of supramolecular chemistry has focused on the difference between the bond between atoms and the bond between molecules. To some extent, this definition is intellectually cyclic in that both molecules are defined in terms of collection of "particles (stoms or molecules) that behave as a unit so that it is the perception of the unit that determines whether we consider atoms bonded or not.

Terms referring to type of bonding interactions between atoms, such as dispersion, hydrogen bonding, dipolar bonding, covalent and ionic forces are not often essential to the structural and reactivity issues under consideration. More often chemists are interest in correlations of collections of atoms in space and time. The spatial correlations between atoms, as determined by experiment (X-Ray, spectroscopic, chemical data), are often interpreted in terms of particular types of bonding interactions, but the argument for bonding is cyclic: a given spatial relationship implies a certain bonding interaction and a certain bonding relationship implies a certain spatial relationship. However, only the spatial relationships are subject to direct experimental verification. For example, a tetrahedral spatial relationship of atoms around a carbon atom implies that the carbon atom is sp^3 hybridized, but the hybridization is defined by the tetrahedral arrangement.

Consider the dynamic feature of spatial relationships which are often used to characterize covalent bonding. Covalent bonds are characterized by a correlated directionality of the configuration of atoms that is preserved in time. However, the bond between two carbon atoms in hydrocarbons would usually be considered as covalent yet depending on the structure and reaction conditions, may be broken and reformed on a time scale comparable to that of conformational interconversions. For example, a very stabilized carbon radical or one

that possesses large steric effect toward combination, may exist in rapid equilibrium with it molecular "dimer".

All of this is not intended to dimish the usefulness of the covalent bond as the signature of a molecular collection of atoms. However, the above discussion does provoke consideration of how to define and discuss the characteristics of molecular systems in a manner that is as general as possible in the hope that such a discussion will lead to new insights which in turn will lead to the design of novel chemical systems.

It is the purpose of this report to explore the characterization of molecular systems in terms that will allow the "supramoleclular" characteristics of a collection of atoms to be revealed in a manner that is related to some experimental measurement. The basic idea would be to define a "suprisal" parameter, possessing a value between 0 and 1, which would characterize a system as "totally molecular" (suprisal of 0) or "totally supramolecular" (suprisal of 1). In the analysis a number of terms that are commonly used by physical chemists to collections of photon (electromagnetic radiation), but not by organic chemists to collections of atoms, come to play: correlations, coherence, phase. Clearly a supramolecular photochemist should be concerned with possible useful analogies between collections of photons and collections. Is there for example a "superphotonic" chemistry which is analogous to "supermolecular" chemistry? We shall shuttle back and forth between the language and experiments of light and its photonic component, and matter and its atomic component to seek insights that can enrich and integrate the fields of supramolecular chemistry and photochemisty.

Supramolecular Chemistry and the Aufbau Priniciple

Chemists are accustomed to "Aufbau" principles in dealing with structures. What ever the level of complication of structure the mathematical concepts of composition, constitution, configuration and conformation provide the bedrock of the thinking process. Conformation and constitution refer to the qualititive or topological aspects of structure and configuration and conformation refer to the quantitative or geometric aspects of structure.

For example, concern the terms electron, atom, molecule, supermolecule (or supramolecular assembly). Chemically, the atom is a connected set of electrons, the molecule is a connected set of atoms and the supermolecule is a connected set of molecules. It is up to the chemistry to determine the relevance of the word connected. In each case a standard for comparison of the previous level of structural complexity must be defined. For example, the characteristics of a "free electron" can serve as the standard against which to pit the the characteristic of an electron in an atom; the characteristics of a "free

atom" can serve as the standard against which to pit the the characteristic of an atom in a a molecule; the characteristics of a "free molecule" can serve as the standard against which to pit the the characteristic of an atom in a a supermolecule. To a certain extent the movement from one level of complexity to the next level depends on measurements of the "suprisal" of the system, that is the degree to which some measurement deviates from expectation based on the lower level model.

Chemical physicists have developed the concept that all chemical systems at all levels can be treated in pure mathematical terms and in prinicple all observed properties can be computed from first principles by application of mathematics. This is done by assuming a model, for example, of a structure which includes all the terms contributing to the energy of the structure. This is called "writing down the Hamiltonian" of the structure. Once the Hamiltonian is "written" it is a matter of computation of the observable. However, what often is not recognized is that even if the computation is exact, the result may be meaningless if there are critical terms left out of the Hamiltonian, i.e., in most cases of complexity, one is forced to deal with a truncated Hamiltonian. Unfortunately, all too often those making the calculation of observables do not realize that they are dealing with truncated Hamiltonians!

Lets give some examples. If electronic interactions in an atom are ignored, one can make precise computations which have a certain value, but these computations cannot help very much in determining the "surprisal" due to interelectronic interactions of an atom. Similarly, if intermolecular interactions in a supermolecular system are ignored, one may be able to make precise computation which have a certain value, but these computations cannot assist in understanting the structure and bonding in supramolecular assemblies. In this point of view on can inspect the other guy's Hamiltonian and decide the level of complexity which is being applied and compare it to your own.

With this background we can consider the question, "What comes after the supermolecule and supramolecular assemblies". An obvious, straight forward and important response is "super"supermolecules or "super" supramolecular assemblies. However, in this manuscript we propose to consider a concept that allows the consideration a terms that may be missing in the Hamiltonians of systems at any level of complexity and therefore take the system to a level of complexity that is "sideways" rather than "vertical". We shall use the terms "ultraelectronic", "ultraatomic", "ultramolecular" and "ultrasupramolecular" to describe systems for which static or oscillating electric and magnetic fields are included in the Hamiltonian. The static and oscillating field may be applied externally by the experimenter as electromagnetic radiation or laboratory electrostatic or magnetic fields.

In addition, electric and magnetic fields which result from the components of the system at the atomic and molecular and supermolecular level also occur.

Examples of Übersupramolecular Photochemistry

In this report we consider specifically examples of surprisals in ultrasupramolecular chemisty, i.e., cases where the application of electric and magnetic fields causes supramolecular systems to have suprising chemical or physical properties when considered from the standpoint of a model for which such fields are absent from the Hamiltontian.

In particular we shall consider examples from the field of "complex fluids" (micelles in aqueous solution) and "porous solids" (zeolites). We shall explore how "atomic resonances" in space and time possess an analogy to "photonic resonances" in space and frequency. This analogy has the amusing and provocative flavor of a mathematic inverse transform whereby one system is "topologically transformed" into another and also has the important feature of forcing the overlap of two apparently orthogonal paradigms to see if analogies can lead to meaningful insights that will enrich the field of supramolecular chemistry.

Non-covalent synthesis of large supramolecular assemblies

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Non-covalent interactions that are formed in a reversible manner are the tools in chemistry and biology to program individual molecules in such a way that larger structures are assembled without the need to form covalent bonds. These individual molecules should contain all chemical information to render the assembly process unique. There are several ways to achieve this goal and the work in our group is focused on two of the possibilities, viz. hydrogen-bonded aggregates[1] and metallodendrimers[2].

In the area of hydrogen-bonded aggregates one of the fundamental problems is that the individual bonding interactions are weak and that multiple hydrogen bond acceptors and donors in one molecule render these extremely insoluble. We have circumvented this problem by the assembly of at least nine molecules in a circular molecular box-like structure. This has the advantage that the individual components with only three or six hydrogen bond donors and acceptors are still sufficiently soluble in organic solvents, but that the ultimate aggregate is held together by 36 hydrogen bonds. Such aggregates with "molecular" weights as high as 15.000 D have been characterized by X-ray analysis, NMR spectroscopy and mass spectrometry.

In an alternative way we use coordinative interactions between organic ligands and metal centres (Pt, Pd) incorporated in so-called pincher structures. These building blocks can (self)assemble upon the removal of a protecting, kinetically stable, ligand at the coordinated metal centre. Assembly can occur in a divergent or convergent fashion, in analogy with the synthesis of

dendritic structures via covalent bonds. Via the divergent approach, particles with a narrow size distribution between 200 and 250 nm can be obtained in a one-step procedure. A step-wise convergent assembly process leads to metallodendrimers with molecularly defined nanostructures with a diameter of 15 nm and molecular weights up to 100.000 D.

Recently we have shown that non-covalent synthesis of such structures is also possible via a combination of the hydrogen bonding and coordination chemistry. Our results show that non-covalent synthesis methods are extremely suitable for the assembly of nanostructures and that supramolecular chemistry can be regarded as one of the most promising enabling technologies for the construction of nanostructures.

Introduction of functions in these nanostructures is the next target in our work.

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HYDROGEN BONDING MOTIFS FOR THE FORMATION OF SELF-ASSEMBLED STRUCTURES

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In this lecture we will place particular focus on the development of small organic molecules that use hydrogen bonding groups to stabilize well-defined aggregates in solution and in the solid state. We have previously described the synthesis of different urea benzoate derivatives (e.g. 1 and 2) in which the hydrogen bonding groups are positioned at varying positions around the ring. We showed by X-ray crystallography and NMR that these derivatives form aggregates, the shape of which is controlled by the position of the hydrogen bonding groups.

1a = R = C$_4$H$_9$ 2a = TMA salt
1b = R = C$_{10}$H$_{21}$ 2b = TBA salt
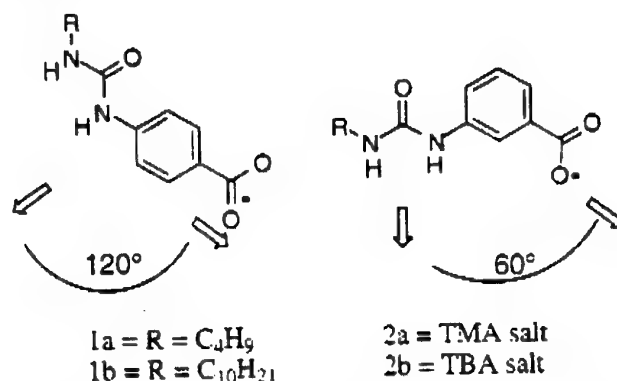
Recently, we have extended this work to include corresponding monomeric subunits based on 2-aminopyridine-carboxylic acid in place of the urea carboxylate pair. The 2-aminopyridine carboxylic acid groups can engage in a bidentate hydrogen bonding interaction (Figure 1) very similar to that seen with the urea carboxylates. The advantage of the pyridine systems is that solubility is often improved and the absence of counter ions (to balance the carboxylate ion) simplifies analysis of the interaction both in solution and in the solid state. We have carried out extensive investigations of the solution behavior of 2-acylaminopyridine-5-carboxylic acid (3) and 2-acylaminopyridine-6-carboxylic acid (4) and have shown that the intermolecular aggregation depends
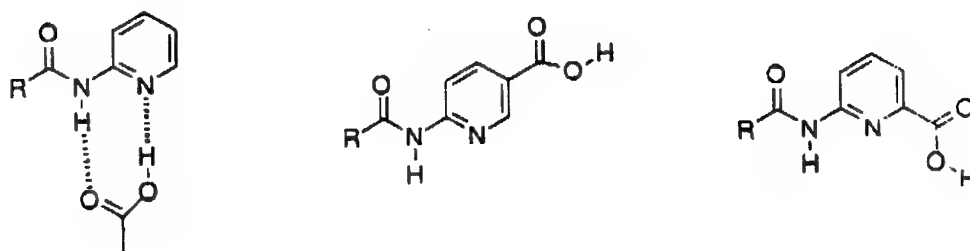

Figure 1   **3**   **4**

critically on the orientation of the two hydrogen bonding substituents. In the case of 2-acylaminopyridine-6-carboxylic acid (4), ^{1}H NMR dilution experiments and vapor phase osmometry point to the formation of a cyclic trimeric aggregate in CHCl$_3$ solution with a likely structure corresponding to 5. In the solid state, X-ray crystallography shows that a linear ribbon aggregate is formed corresponding to 6. In both cases bidentate hydrogen bonding is the organizing force for aggregate formation. However, in solution cyclization appears to be favored over infinite ribbon formation. This can be understood in terms of entropy since in the case of 5 six hydrogen bonds are

formed from the association of six particles, whereas with **6** the entropically unfavorable association of a fourth molecule must occur before three pairs of hydrogen bonds are formed.


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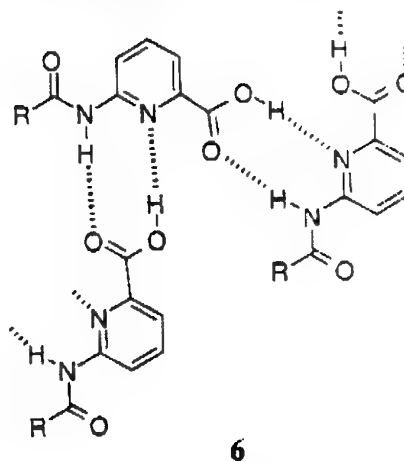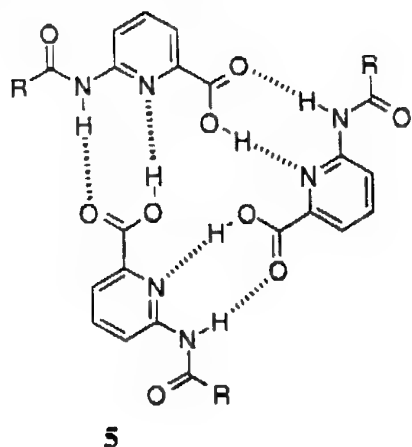
In the case of 2-acylaminopyridine-5-carboxylic acid (**3**), the ^{1}H dilution data is less clear but points to very different behavior from that of **4**. Non linear regression analysis of the sigmoidal change in chemical shift as a function of concentration is consistent with the aggregation of five molecules in solution to form, presumably, a cyclic pentamer of type **7**. Once again, X-ray crystallography shows that an infinite linear ribbon (such as **8**) is preferred in the solid state. However, the key role of intermolecular hydrogen bonds in controlling aggregation is confirmed as is the very different behavior for the two substitution isomers of the pyridine carboxylic acids.

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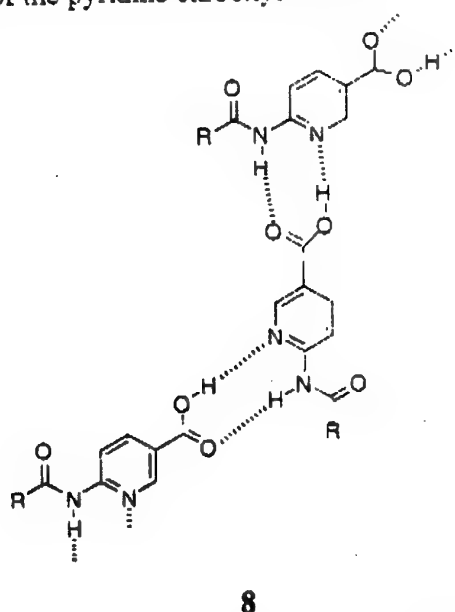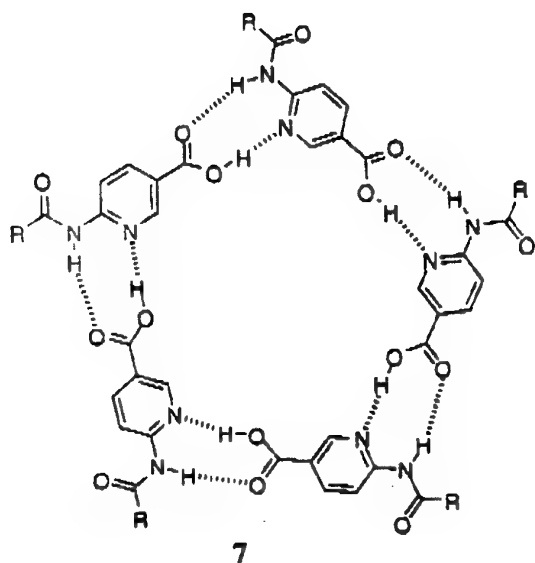
We have recently extended this work with the synthesis of a dimeric 2-acylaminopyridine-6-carboxylic acid derivative in which two hydrogen bonding monomers are separated by a rigid xanthene spacer **9**. Preliminary results show that long chain acylamino derivatives of **9** are soluble in CDCl₃ and show aggregation behavior consistent with the formation of a double stacked cyclic trimer of type **10**. This strategy is particularly interesting for the formation of discrete aggregates in solution since they can be readily functionalized on the exterior (through the acylamino group) and can also lead to aggregates (derived from analogous derivatives of **7**) with a capacious interior.

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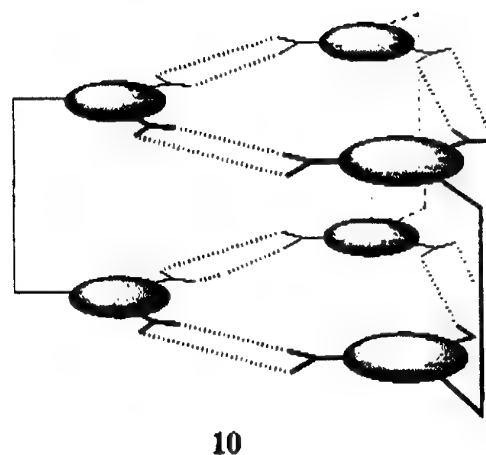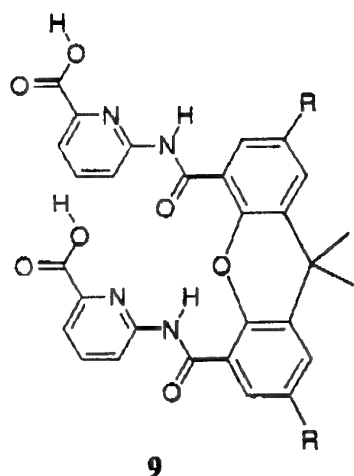
We have also shown that 5-decyloxyisophthalic acid derivatives form discrete hexameric aggregates with an internal cavity of 14Å, as shown in **11**. The 2-position of the benzene ring can be functionalized to project different substituents into the center of the cavity. We will further describe our attempts to extend this strategy by changing the angle between the hydrogen bonding sites which should lead to a change in the aggregation number. The 2,5-dicarboxylic acid derivatives of 5-

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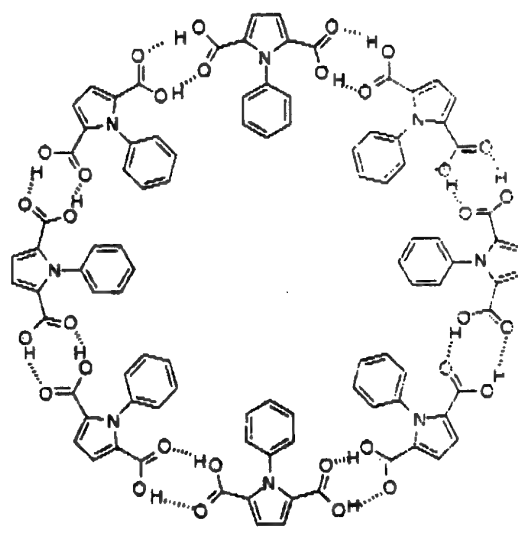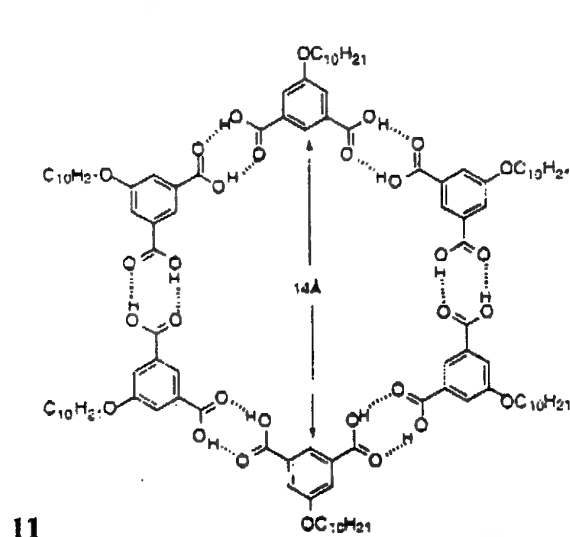
membered aromatic rings (furan, thiophene and pyrrole) have a 135° angle between the substituents and thus the potential for self-associating as octamers. We are testing this possibility with pyrrole-1-phenyl-2,5-dicarboxylic acid. The structure for the potential aggregate of pyrrole-1-phenyl-2,5-dicarboxylic acid is shown in **12** and confirms schematically that a self-associated octamer can form with undistorted bidentate hydrogen bonds between the substituents. The structure also shows the projection of all eight phenyl groups into the center of the cavity with a later potential for functionalization.

Hydrogen bonds in organized monolayers

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1. Introduction

Among the various intermolecular interactions, hydrogen bonds play an important role in arranging different molecules to large supramolecular assemblies. Prominent examples are found in biopolymers where hydrogen bonds contribute strongly to determining the tertiary structure of proteins and control base pairing of nucleic acids. A large field with a major contribution of hydrogen bonds is molecular recognition in biosystems like antibody-antigen interactions. Studies of molecular recognition in organized molecular assemblies like monolayers, vesicles and micelles have recently been reviewed [1]. The main difference between H bond interactions and electrostatic interactions between charged molecules aside of the magnitude is the directionality of H bonds. Therefore, molecules can form H bonds in particular geometries only. This feature opens possibilities to organize different molecules in a well defined way to hetero-dimers or extended aggregates. Organized monomolecular layers at the air-water interface and as components of monolayer systems on solids are excellent model structures for mechanistic studies as well as for the construction of artificial devices capable of molecular recognition using hydrogen bonds. An important phenomenon here is the competition in hydrogen bond interactions with the recognition site between the target molecule and water. A large variety of investigations has been performed using different H bond donors and acceptors to mimick the interactions observed in biosystems. A small selection of examples is given in the following along with the results of some recent investigations.

2. Base Pairing Interactions

Monolayers of an amphiphilic diaminotriazine are capable of selectively binding nucleosides as well as nucleic acid bases dissolved in the aqueous subphase [2]. Evidence for binding was obtained from FTIR reflection spectra of multilayer systems (LB-layers) assembled by monolayer transfer onto glass slides covered with a 100 nm thick vapor-deposited gold film. Additional quantitative binding data from X-ray photoelectron spectroscopy confirmed these observations. Clearly, a selectivity was found with binding of thymidine, uridine and thymine in preference of adenosin and adenine, respectively. This seems to be due to the fact that the former group of bases and nucleic acids form 3 H bonds per base with the amphiphilic diaminotriazine, whereas adenin and adenosin form 2 H bonds per base only.

A variety of amphiphiles with nucleobases and nucleosides have been synthesized and the interaction of monolayers of these materials with monomeric as well as polymeric nucleobases have been studied [3]. Complementary nucleobases dissolved in the subphase expand the monolayer more than non-complementary bases. The effect of monomeric bases on the surface pressure-area (π-A) isotherms is much smaller than that of the polymeric bases, demonstrating again the necessity of a minimum number of H bonds per base to be formed or cooperative interactions for binding by a monolayer at the air-water interface.

3. Multisite Recognition

A molecule like flavine adenine dinucleotide (FAD) provides different sites for formation of H bonds and ionic interactions. In an elegant work, this has been used to achieve molecular patterning and multi-site recognition, respectively, in a mixed monolayer of two [4] or three different amphiphiles [5]. The binding of FAD has been characterized by the changes of the surface pressure-area isotherm in the presence of FAD in the aqueous subphase as well as by IR and XPS spectroscopy of transferred multilayer systems on solid support. Most striking is the difference between the scanning force microscopic images of the two-component mixed monolayers on the aqueous subphase in absence and in presence of FAD, see Figure 1 [4].
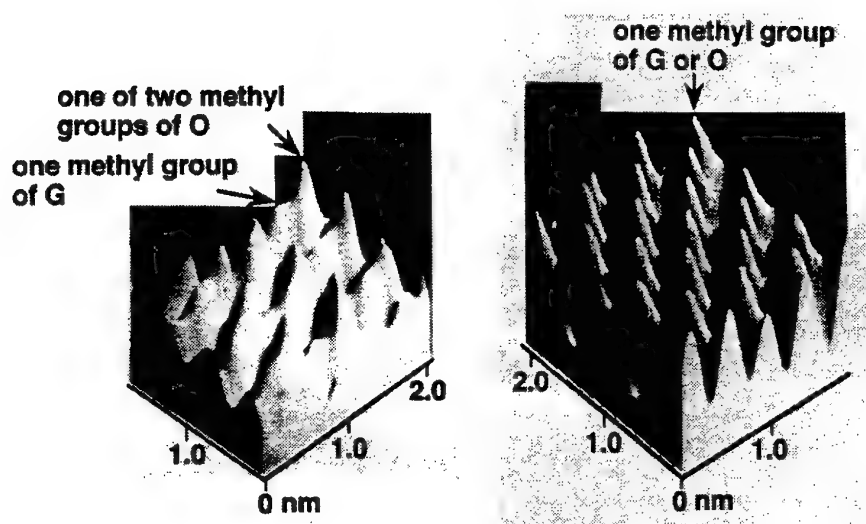

Figure 1: SFM image (1.8 x 2.1 nm²) of a mixed monolayer of G and O, molar ratio 1:1, on an aqueous subphase with FAD (left) and on pure water (size 1.9 x 2.1 nm², right); reproduced from ref. [4].

The monolayer components, octadecyl-guanidinium G, and di-octadecyl-orotate O, are laterally rearranged due to specific recognition by FAD. The methyl end group of G is at a height different from that of methyl end groups of O.

4. Large Aggregate Formation

Hydrogen bonds play an inportant role in protein interactions. The efficient molecular recognition in biosystems has been adapted to use in artificial structures such as monolayers. An example is the strong interaction between biotin and streptavidin with biotinylated lipids in the monolayer and streptavidin in the aqueous subphase [6]. Based on the fact, that streptavidin that has four binding sites, this specific interaction has recently been used to form two-dimensional aggregates in monolayers of a tetrabiotinylated porphyrin via binding of streptavidin from the subphase [7].

Well defined extended aggregates have been formed in organic solution by hydrogen bond interactions of two different molecules, like barbituric acid and 2,4,6-triaminopyrimidine (TAP) [8,9]. This system with numerous H bonds per TAP molecule forming extended molecular strands is particularly suited for studies in monolayers at the air-water interface.

Amphiphilic derivatives of barbituric acid have been used for a spectroscopic investigation of the hydrolysis of this derivative in organized monolayers due to binding of TAP [10]. The barbituric acid derivative (ABA) forms associates as concluded from the reflection spectrum of the monolayer. These associates disappear upon binding of TAP from the aqueous subphase (see Figure 2, left) at bulk pH = 3. At this pH no hydrolysis occurs, however at a bulk pH = 6.5 the disappearance of the main band in the reflection spectrum at 460 nm indicates hydrolytic cleavage of the C=C bond of the chromophore (retro-Knoevenagl reaction) with formation of barbituric acid and the corresponding amphiphilic aldehyde as characterized by the new band with maximum at 350 nm (see Figure 2, right).
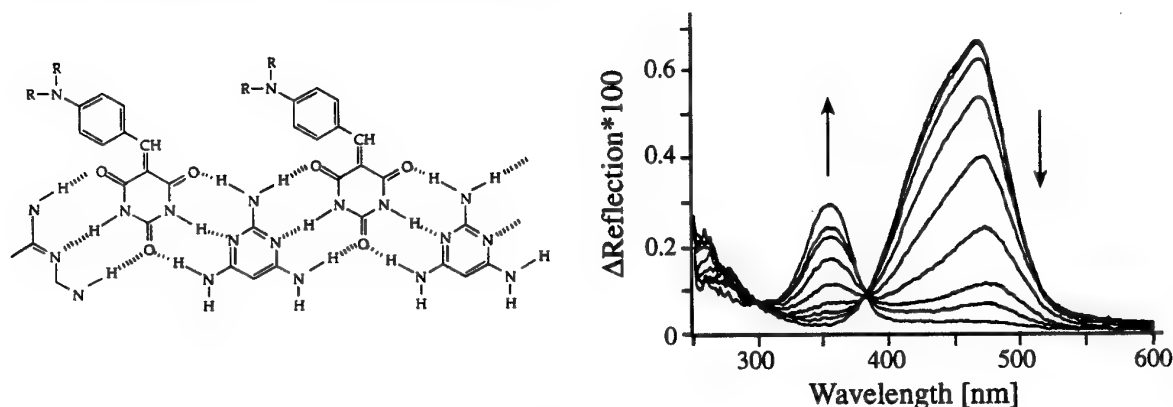

Figure 2: Structures of the amphiphilic derivative of barbituric acid, ABA, and formation of molecular strands by incorporation of 2,4,6-triamino-pyimidine, TAP, from the aqueous subphase (left); reflection spectra (right) of a monolayer of ABA on 10^{-4} M TAP, pH = 6.5; the band at 460 nm decreases and that at 360 nm increases with increasing time: hydrolysis of ABA (λ_{max} = 460 nm) and formation of the corresponding aldehyde (λ_{max} = 350 nm); reproduced from [10].

In the absence of TAP, a very slow hydrolysis is observed at bulk pH = 10 with formation of the aldehyde. These observations clearly show that TAP binds to the head group region of the

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monolayer of the amphiphilic derivative of barbituric acid. This is possible by formation of hydrogen bonds only. The C=C double bond is activated by the H bond to TAP, and therefore, TAP catalyzes the hydrolysis.

The ratio of the amphiphilic barbituric acid ABA and TAP may be strictly defined by co-spreading of both at the air-water interface. Although TAP is quite soluble in water it remains in the monolayer due to ist interactions with ABA. For a molar ratio of ABA:TAP = 3:1, each TAP molecule caralyzes the hydrolysis of two ABA molecules. Since the barbituric acid formed and the TAP are no longer anchored in the monolayer, they dissolve in the aqueous subphase. Consequently, the reaction stops after hydrolysis of 2/3 of the ABA in the monolayer [10].

Aggregates of TAP and barbituric acid form also in aqueous solution. Cleavage of ABA at the air-water interface is observed on a subphase containing a 1:1 aggregate of TAP and barbituric acid (10^{-4} M, pH = 6.5), although much slower than in the case of a subphase containing only TAP at same concentration and pH [11]. Monolayers of an amphiphilic derivative of 2,4,6-triaminotriazin (melamine), bind barbituric acid from the aqueous subphase at a ratio of (1.1 ± 0.1):1. After transfer on mica, such complex monolayers show a very regular molecular packing in the scanning force microscope in reasonable agreement with packing of alkyl chains [12].

5. Combination of Hydrogen Bonds with Ionic Interactions

Particularly strong interactions can be expected in the case of a combination of directionally controlled hydrogen bonding with attractive electrostatic forces, i.e. ion pairing. Indeed, formation of infinite molecular tapes has been observed even in aqueous solution by self-assembly of complementary dianionic and dicationic hydrogen bond donors and acceptors [13]. Evidence for such interactions in monolayers at the air-water interface is obtained from π-A isotherms of mixtures of the amphiphilic diamidine THA (structure see Figure 3) and terephthalic acid TPS as well as nitro-isophthalic acid, NIP. The monolayers were formed by co-spreading of the components. Figure 3 shows π-A (full lines) and surface potential-area (ΔV-A, dotted lines) isotherms of monolayers of the pure THA (1,1'), and of mixtures THA:TPS = 1:1 (2,2') and THA:NIP = 1:1 (3, 3'). A is the area per THA molecule spread. The presence of terephthalic acid, TPS, as well as nitro-isophthalic acid, NIP, clearly modifies the π-A and ΔV-A isotherms of THA. The collapse pressure is strongly increased, and the surface potential is considerably diminished in the mixed monolayers. In case of the mixed monolayer THA:TPS the area per THA molecule at π = 10 mN/m is 1.53 nm^2 (curve 2) which is in excellent agreement with an area of 1.5 nm^2 estimated for the pair THA/TPS from X-ray crystallographic data [13] assuming dense packing of parallel strands of THA:TPS = 1:1. The reduction of the surface potential at 10 mN/m comparing THA:TPS with = 1:1 THA is $\Delta\Delta$V = -0.067 V. Such a reduction may be attributed to salt formation in the monolayer plane (no contribution to the surface potential) in the mixed monolayer strongly diminishing the contribution of the diffuse double layer present in

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the case of the pure THA monolayer to the surface potential (measuring the normal component of dipole moments only).
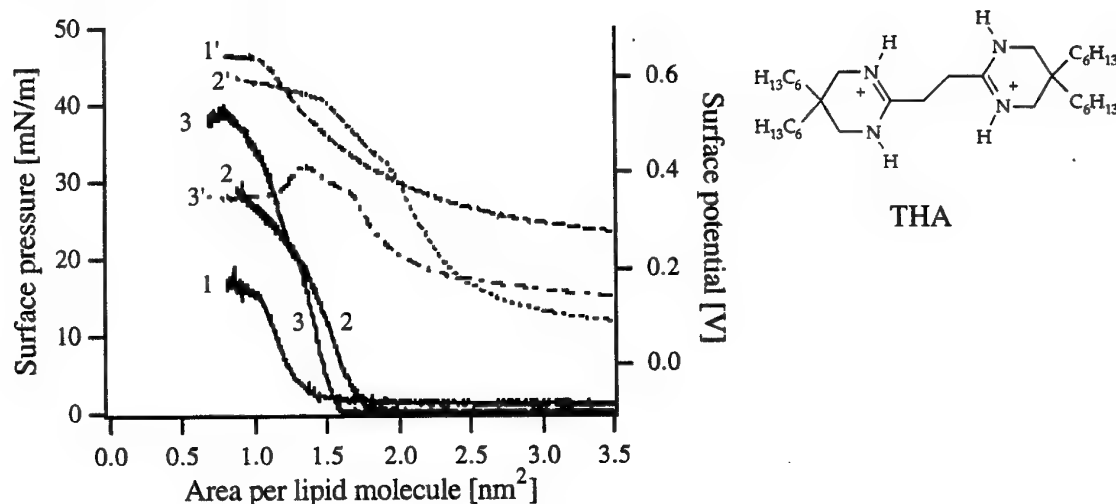

Figure 3: Surface pressure (π, full lines) and surface potential (ΔV, dotted lines) plotted vs. area per THA molecule, A, of monolayers of THA (1, 1') and of mixtures THA:TPS = 1:1 (2, 2') and THA:NIP = 1:1 (3, 3'); subphase water, 20°C (left); Structure of THA (right).

The behavior of the mixed monolayer THA:NIP = 1:1 is similar to that of THA:TPS. The area per THA is A = 1.42 nm². The surface potential is more strongly reduced in the presence of NIP, i.e. $\Delta\Delta V$ = -0.202 V, indicating an additional influence of the nitro group as compared to the case of THA:TPS.

The modification of both π-A and ΔV-A isotherms of THA due to the presence of terephthalic acid and nitro-isophthalic acid, respectively, in the spreading solution clearly demonstrates that these components are present in the monolayer at the air-water interface. This may be confirmed by spectroscopic measurements of the monolayers. The mixed monolayers have been transferred onto quarz plates at a surface pressure of 10 mN/m. Figure 4 shows the absorption spectra (measured as difference in transmission of a reference section of the slide without the monolayer and the sample section with the monolayer) of single monolayers of THA:TPS = 1:1 (curve 1) and of THA:NIP = 1:1 (curve 2).

The monolayer of THA:TPS = 1:1 shows a maximum around 209 nm and another band with maximum at 240 nm. In solution, the main absorption band of TPS is at 233 nm (another small band at 285 nm) and that of THA is at 222 nm. Therefore, we attribute the band at 209 nm mainly to THA and the band at 240 nm to TPS. The monolayer of THA:NIP = 1:1 shows a strong band with maximum at 210 nm and a weak band at 250 nm. In solution, NIP has a band with maximum at 225 nm and a weaker band at 255 nm. Consequently, the band at 210 nm is due to both THA and NIP, whereas the weak band at 250 nm is attributed to NIP. The shifts observed in the monolayers may be caused by interactions between the components as indicated by slight deviations of the spectra of the mixtures in solution from additivity. The absorption

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spectra of single monolayers on quartz reconfirm the presence of terephthalic acid and of nitro-isophthalic acid in these monolayers based on H bonds and electrostatic interactions with THA.
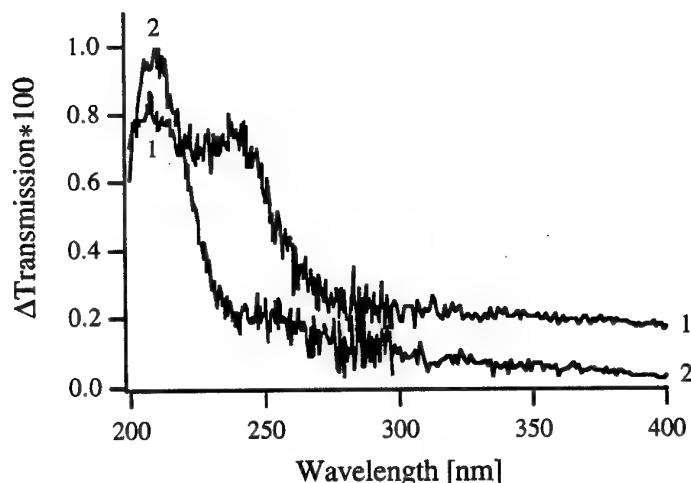

Figure 4: Absorption spectra of single mono-layers transferred on quartz plates; (1) THA:TPS = 1:1; (2) THA:TPS = 1:1; the absorption here is the difference in transmission ΔT between a reference section of he slide without monolayer and the sample section with monolayer.

From the absorption ΔT at the maximum, the surface density σ of the absorbing species can be calculated in a first approximation from the extinction coefficient ε in solution assuming that this is unchanged [14,15] according to

$$\sigma/(\text{nm}^{-2}) = [6.023 \cdot 10^{23} \cdot \Delta T]/[f_o \cdot 2.303 \cdot \varepsilon/(\text{Lmol}^{-1}\text{cm}^{-1}) \cdot 1000 \cdot 10^{14}] \tag{1}$$

where f_o is a factor taking the different average orientations of the transition moment in the monolayer as compared to the solution into account. For an orientation of the transition moments in the layer plane, $f_o = 1.5$. With the extinction coefficients measured in the mixed solutions the values $\sigma = 0.37$ nm^{-2} is obtained for TPS as compared to $\sigma = 0.65$ nm^{-2} calculated from the π-A isotherm. In the case of NIP the values are $\sigma = 0.59$ nm^{-2} (absorption spectro-scopy) and $\sigma = 0.70$ nm^{-2}. This calculation reconfirms the conclusion based on the isotherm measurements that both TPS and NIP are present in the mixed monolayers.

6. Conclusion

H bond interactions in monolayers, sometimes in combination with electrostatic interactions, give rise to molecular patterning, molecular recognition, binding of a catalyst and the formation of large ordered aggregates. Truely supramolecular structures are spontaneously formed in monolayers at the air-water interface due to the directionality of the H bond interactions.

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FUNCTIONAL SUPRAMOLECULAR ARCHITECTURES
ON SURFACES

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As part of studies on the early steps of crystal nucleation from a structural view point, we investigated the organization of molecules into supramolecular architectures at the air/solution interface by applying surface sensitive analytical tools such as grazing incidence X-ray diffraction (in collaboration with K. Kjaer and Jens Als Nielsen), scanning force microscopy , cryo transmission electron microscopy etc.

In this lecture we shall describe the formation of crystalline multilayers at the air side of the interface. In particular we shall focus on systems, where a water insoluble amphiphile interacts with a water soluble ion or molecule to form crystalline architectures at the interface. The following systems will be considered:

a) The self-organization of bolaamphiphilic molecules of type $X-(-CH_2)_n-Y$ where $X=Y = - CO_2H$; $X = OH$; Y_2CO_2H or related systems on aqueous solutions of inorganic salts into crystalline oriented thin films. The use of such films, for the preparation of semiconductor quantum particles will be illustrated with representative examples. In particular we shall focus on systems that form organic/inorganic composite materials, where inorganic semiconductor particles are arranged in superlattices within the organic matrix.[1,2,3]

b) The formation of organometallic architectures, such as silver or cobalt grids at the air solution interface. (work done in collaboration with the group of Prof. J.M. Lehn in Strasbourg).[4]

c) The formation of channel-like structures of salts of valinomycin and non-actin within phospholipid monolayers.[5]

d) The formation of interdigitated trilayers of mandelic acid/phenethyl amines, or mandelic acid with α-hydroxyphenyl amidinium salts. The role that such structured films can play as self-replicating systems will be presented.[6]

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SUPRAMOLECULAR SYNTHESIS OF ORGANIC AND METAL-ORGANIC LAMINATES WITH AFFINITY FOR AROMATIC GUESTS: HYDROPHOBIC CLAY MIMICS

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ABSTRACT Examples of crystal engineering of new laminated structures based upon purely organic or metal-organic materials will be presented.

1. Introduction

Crystal engineering offers the intriguing promise of facile development of a new generation of functional solids which have been designed from first principles. Therefore, a degree of control over bulk properties that is not inherently present in naturally occurring compounds is potentially offered. The relatively recent rise in interest in the concept of crystal engineering[1,2] owes much to advancements in supramolecular chemistry and recognition, understanding and exploitation of *supramolecular synthons.*[3] A property of solids that has attracted considerable attention from chemists and crystal engineers is the ability of a solid to adsorb and/or desorb guest molecules. Clays, via intercalation between 2D layers, and zeolites, which contain channels and cavities because of rigid 3D frameworks, are natural prototypes and are of considerable commercial interest because of their widespread applications in separations and catalysis.[4] There are now examples of metal-organic[5,6] and organic[7,8] zeolite mimics which incorporate organic guests and there are also "organic clay mimics" which are able to exchange metal cations.[9] However, there are not to our knowledge examples of hydrophobic clay mimics. In this contribution we report the first examples of this new class of compound, simple organic salts and metal-organic coordination polymers that self-assemble into laminated structures which are structurally related to clays but are inherently hydrophobic because of their chemical nature.

2. Strategy

The concept of *crystal engineering,* originally introduced in 1970 in the context of stereochemical control of photochemical reactions,[1] encompasses all aspects of design in the solid state and therefore has no boundaries in terms of the chemical type of the moieties involved or which intermolecular/ionic forces can be exploited. However, although even the weakest of noncovalent interactions are directional enough to be exploitable, coordination polymerization involving transition metals would seem to offer a particularly strong opportunity for chemists to directly impact materials science. The "golden rule" of crystal engineering is that the driving force for formation of crystals is self-organization. This idea is especially appropriate for organic salts or coordination polymers. The former are particularly relevant as organic salts can form very strong charge assisted hydrogen bonds with predictable motifs. The latter can generate 1D, 2D or 3D architectures with a reasonable degree of control and

predictability because metal coordination geometries are so well documented and understood. Both classes of compound are inherently modular and they are discussed separately below.

2.1 "Organic Clays"

Trimesic acid, H_3TMA, and trimellitic acid, H_3TML, are two inexpensive and thermally and chemically robust carboxylic acids with exodentate functionality in two dimensions. They are therefore ideal templates for generation of 2D hydrogen bonded arrays.[10-16] $[NR_2H_2]_2[HTMA]$ and $[NR_2H_2]_2[HTML]$, which are afforded in simple one-pot processes by the appropriate acid-base reaction in MeOH or EtOH, exhibit such structures because of the complementary nature of the strong hydrogen bond donors of the cations and the strong hydrogen bond acceptors of the anions. For R = propyl, hexyl, octyl or decyl interdigitated laminates with poor ability to incorporate guest molecules are formed.[16] However, if R = benzyl, interdigitation is eschewed in favour of incorporation of solvent or aromatic guest molecules. X-ray crystallographic characterization of 23 host-guest complexes based upon $[N(benzyl)_2H_2]_2[HTMA]$ or $[N(benzyl)_2H_2]_2[HTML]$ hosts has revealed that aromatics as diverse in size and electronic character as nitrobenzene, anisole, veratrole, 1,4-dimethoxybenzene, 1,3,5-trimethoxybenzene, m-xylene, mesitylene, tetramethylbenzene, pentamethylbenzene, hexamethylbenzene, dibenzylamine, naphthalene, 1-methylnaphthalene, pyrene and ferrocene can be incorporated as guests by intercalation. Whereas the connectivity of the hydrogen bonding networks that occurs within the laminates, Fig. 1, shows little variation, it is adaptable enough to permit at least three basic crystal packing modes, exemplified by the structure presented in Fig. 2. For 22 of 23 compounds the proportion of guest varies from 16.6% to 26.3% by mass and is based upon the relative size of the guest molecule and the packing mode adapted by the laminates. The unit cell lengths in these 21 compounds are based upon multiples of ca. 12 x 17 x 21Å. The 12Å distance represents the approximate interlayer separation whereas 17 x 21Å represents the dimensions of the repeat unit within the laminate (Fig. 1). An analogy might reasonably be drawn between the new compounds and lipid bilayers since the former are effectively an infinite stack of hydrophobic bilayers. As might be expected,[17] interactions between guest molecules and the host frameworks are based upon a plethora of edge-to-face and face-to-face interactions between various aromatic moieties. In the absence of guest molecules or the presence of a very small number of guest or solvent molecules interdigitation of benzyl groups occurs and interplanar separations are
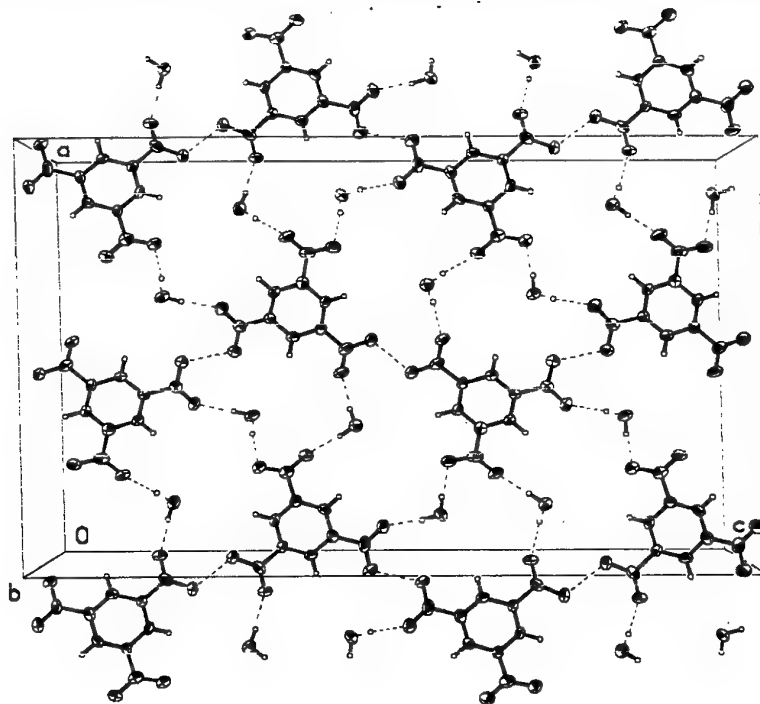
Figure 1. The hydrogen bond network in [NR$_2$H$_2$][HTMA] compounds (R = benzyl, alkyl). R substituents are omitted for the sake of clarity.
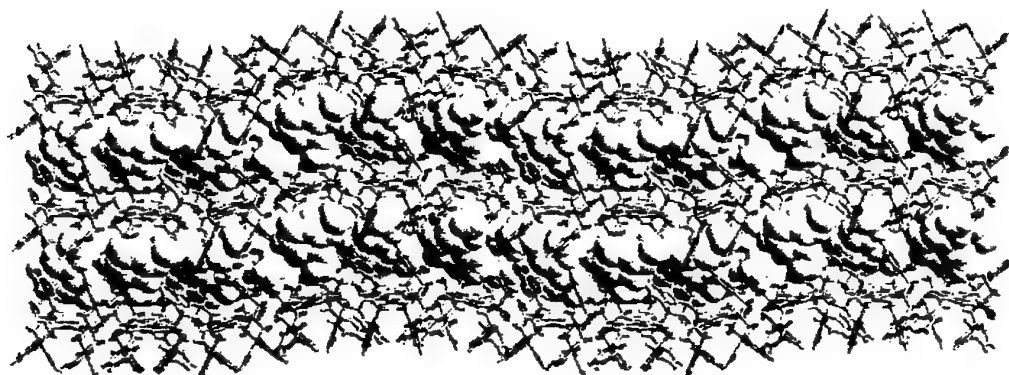
Figure 2. An illustration of the crystal packing in the supramolecular laminate based upon [N(benzyl)$_2$H$_2$]$_2$[HTMA]• veratrole•1/3EtOH, Guest molecules are in space-filling mode. Crystal data: monoclinic, space group P2$_1$/c, a = 11.5765(6), b = 49.905(3), c = 21.505(1)Å, β = 90.929(1)°, V = 12423(1)Å^3, Z = 12, ρ = 1.22 Mgm^{-3}, R = 0.076, Rw = 0.139 for 11030 out of 21508 reflections with I>2σ(I). Data were collected on a Siemens SMART/CCD diffractometer at 193K and the structure was solved and refined using SHELX/TL.

reduced to 8-9Å.[18] Our observations with monoalkylammonium salts will also be reported.

2.2 Metal-organic clays

Our investigations have also focused upon transition metal based laminated structures. As revealed in the schematic below, it is reasonable to envisage a generic class of

compound which is based upon a square planar or octahedral metal and linear "spacer" ligands. The first open framework examples of these compounds were based upon Cd(II) and 4,4'-bipyridine and were reported by Fujita quite recently.[19] Fig. 3 reveals how we have extended this series of compounds so as to include larger open framework coordination polymers which have cavities with an effective cross-

sectional area of 11 x 11 Å. The cavities in these compounds are therefore large enough to enclathrate more than one aromatic guest molecule at a time. Fig. 3 reveals how veratrole (1,2-dimethyoxybenzene) molecules can be trapped inside the cavity. These compounds are also capable of sustaining triple-decker stacks of 1-methylnaphthalene molecules. These compounds and a number of closely related structures will be discussed in detail and we shall present the results of preliminary AFM experiments conducted in collaboration with Dr. A.W. Coleman (IBCP/CNRS Lyon).
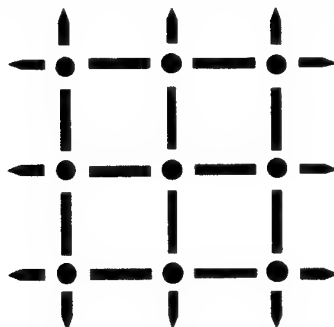
2.3 Supramolecular isomerism.

The issue of supramolecular isomerism in coordination polymers was recently raised by us.[20] We shall present a number of examples of supramolecular isomerism from both organic and coordination polymers and discuss this issue in the context of bulk properties and the closely related phenomenon of polymorphism.

2.4 Applications

We shall present a summary of preliminary experiments that we have conducted in the context of desorption and guest exchange with both classes of compound. We shall also attempt to present a broad overview of the challenges and opportunities that face crystal engineers, in particular possible applications in catalysis, separations science, materials science, polymorphism and solid-state synthesis, including photochemistry.
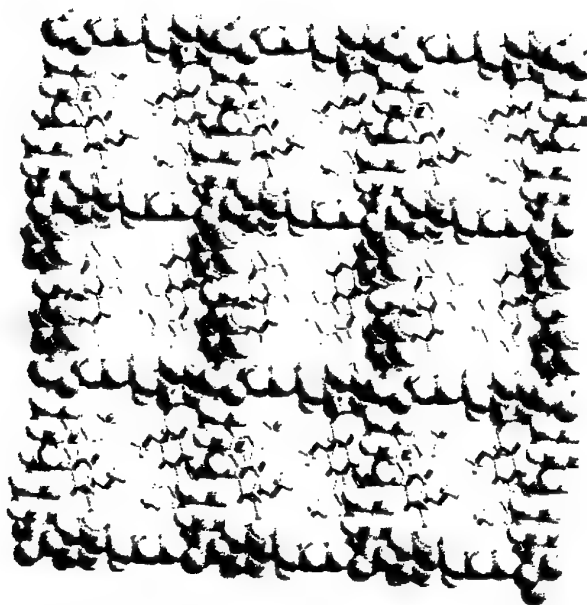
Figure 3. An overhead view of the open framework square grid coordination polymer [Ni(dipy-Et)$_2$(NO$_3$)$_2$]$_n$ · 2 veratrole: 0.10 x 0.20 x 0.20 mm, pale blue rectangular crystal, triclinic, P-1 with a = 12.4022(9), b = 13.5639(10), c = 13.5930(9) Å, α = 61.5050(10), β = 87.1850(10), γ = 89.535(2)°, Z = 2, V = 2006.9(2) Å^3, ρ_{calc} = 1.369 Mgm^{-3}, μ = 0.55 mm^{-1}, 3.28>2θ>55.88°, T = 290K, R = 0.0612, R$_w$ = 0.1604, 4810 out of 8821 reflections with I > 2.0 σ(I) and 518 parameters. Data were collected on a Siemens SMART/CCD diffractometer.

3. Summary

There are several observations that we consider to be of particular relevance. In the case of the organic laminates, the inherent torsional flexibility of the benzyl groups and the ability of even strong hydrogen bonds to distort are manifested by generation of a number of cavity and/or channel geometries for a single host. The ability of the supramolecular laminates to form similar crystalline structures with such a wide range of guests can therefore be rationalized. In the case of both classes of compound, preliminary studies have indicated that guest molecules can be easily removed by heat and/or vacuum to afford a stable amorphous apohost or exchanged by contact with solvent that is rich in another guest molecule. When combined with their low cost, facile supramolecular synthesis, chemical stability and modular nature, this means that the new compounds have potential applications in the context of separations, sensors and as general purpose adsorbents.

In summary, the compounds reported herein are facile to prepare laminated compounds which are sustained by noncovalent interactions, are inherently hydrophobic and, because of their 2D structures and flexibility, have a generic affinity towards intercalation of aromatic molecules. A key feature is that, unlike zeolite mimics, they are selective for chemical type more than size and shape. They therefore complement the stronger shape and size selectivity of 3D structures.

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Crystal Engineering
with
Two-Dimensional Hydrogen Bonding Networks

SUMMARY

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Interest in functional materials based on molecular crystals persists owing to the potential for manipulating solid-state properties by systematic variations of the molecular structure and properties of the molecular components, a principal goal of "crystal engineering". However, attempts at materials design and commonly have been frustrated by an inability to predict solid state structure precisely. A reasonable strategy for surmounting this obstacle is to use robust supramolecular "modules", in which robust is defined as the ability of the module to maintain its dimensionality and general structural features upon changes in ancillary functional groups or other molecular species in the lattice. Robust n-dimensional modules can reduce the crystal engineering problem to 3-n dimensions, thereby simplifying materials design.

Recently we reported molecular layered materials based on a two-dimensional (2D) H-bonded network composed of guanidinium cations (G) and the sulfonate groups of alkane and arene substituted monosulfonate anions (S). The topological equivalence of the guanidinium ions and sulfonate groups, and strong (G)N-H···O(S) H-bonds, favored the formation of quasihexagonal 2D GS networks in more than 30 different crystalline phases containing various sulfonate functionalities. The networks assembled in the third dimension as densely packed bilayers or as continuous stacks of interdigitated single layers due to van der Waals interactions between sulfonate R groups extending from the GS sheets. The pervasiveness of the GS sheets was attributed to their ability to form "accordion" or "pleated" sheets by puckering about (G)N-H···O(S) H-bonding "hinges" joining adjacent 1D ribbons. This puckering, which can be defined by interribbon dihedral angles of $\theta_{IR} < 180^o$, enables the sheets to adapt to the steric demands of different R groups. In a few cases, these steric demands apparently were accommodated further by the formation of a shifted ribbon motif, which still retains five of the original six hydrogen bonds.

The distinctive structural features of the GS networks prompted us to synthesize related materials in which the *mono*sulfonate components were replaced with *di*sulfonates. We anticipated that this would afford pillared bilayer structures, reminiscent of pillared metal organodiphosphonates. This substitution would result in a twofold reduction in alkyl group density, leading to the formation of voids in 2D galleries with sizes, heights, shapes, and chemical environments that could be manipulated by the choice of molecular pillar. The layering motif would depend upon the sizes of the pillar and guest molecules that may occupy these voids. Sterically undemanding pillars and small guests would favor a bilayer motif, whereas large guests would favor a continuous single layer stacking motif. Large
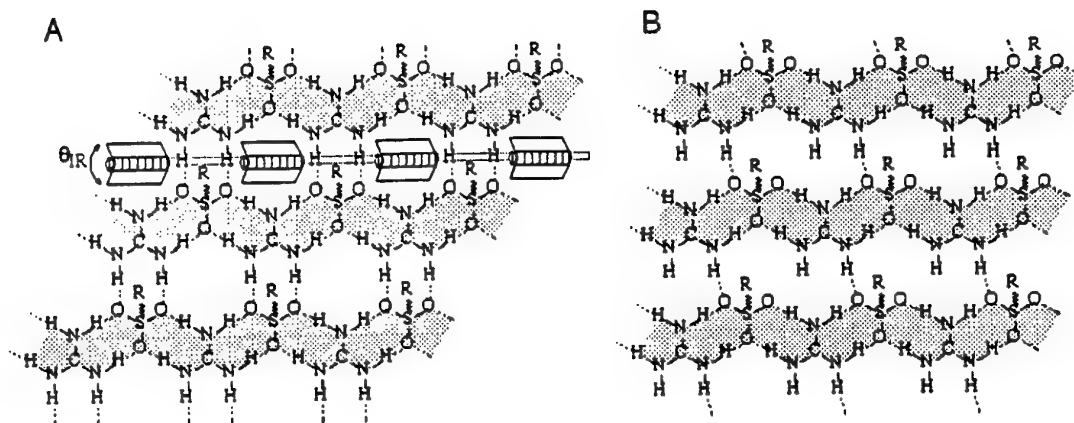
Fig. 1. Schematic representations of the layered hydrogen-bonding motifs observed in guanidinium organosulfonates. One hydrogen-bonded ribbon is shaded, and the hydrogen-bond "hinge" position is indicated in each figure. (A) Quasihexagonal motif. (B) Shifted ribbon motif.
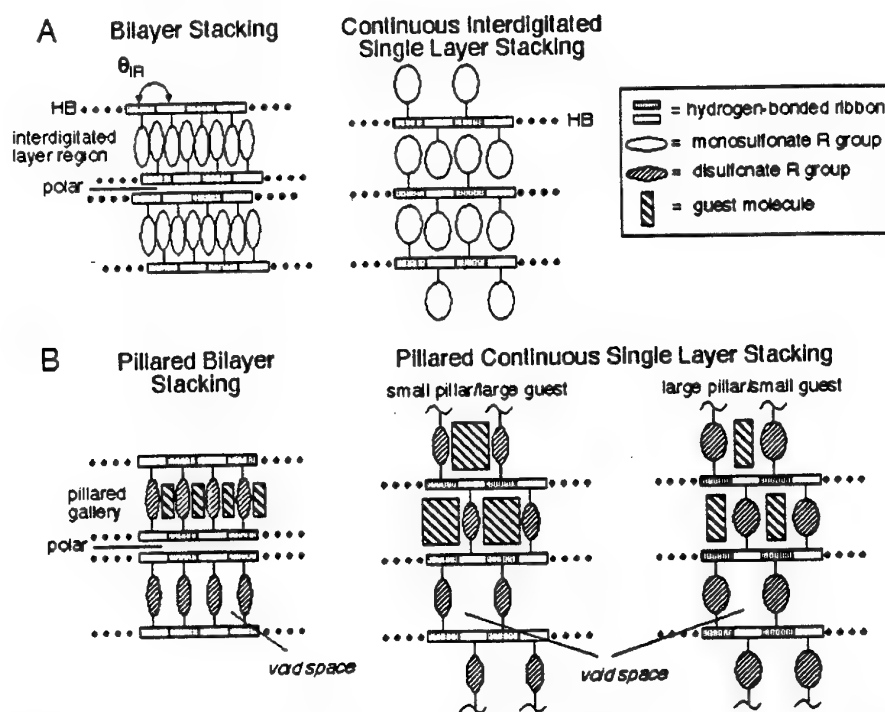
Fig. 2. Schematic representations of layered materials synthesized from **G** cations and alkane and arene substituted monosulfonates and disulfonates, as viewed along the long axis of the H-bonded ribbons contained in the nominally planar **GS** networks. The white and shaded rectangles represent the narrow edges of the ribbons. (A) Two stacking arrangements of the nominally planar **GS** networks observed for **G** monosulfonates. Bilayer motifs are observed for R groups which are small enough to allow interdigitation in the nonpolar region separating the **GS** sheets. If the alkyl or aryl groups are too large, the R groups of adjacent ribbons are oriented to opposite sides of each sheet, which provides room for interdigitation and the continuous single layer stacking of the **GS** sheets. The sheets can adapt further to the steric requirements of the R groups in either layering motif by puckering about (G)N-H···O(S) H-bonding "hinges" between adjacent ribbons (θ_{IR}). (B) Analogous possible layering motifs for **G** disulfonates. The twofold reduction in the number of alkyl groups in the pillared region opens nanoscale voids capable of enclathrating molecular guests. The layering motif is governed by the combined size of pillar and guest. Large guests should favor the "brick motif" in the center even when the pillar is small.

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pillars would favor only single layer motifs with small guests or may even exclude guest molecules. The likelihood of these structures can be deduced from a simple geometric model that compares the area of a guest molecule, as projected onto the **GS** sheet, with the area available between the pillars in the different layering motifs.

The distinctive structural features of the **GS** networks prompted us to synthesize related materials in which the *mono*sulfonate components were replaced with *di*sulfonates. We anticipated that this would afford pillared bilayer structures, reminiscent of pillared metal organodiphosphonates. This substitution would result in a twofold reduction in alkyl group density, leading to the formation of voids in 2D galleries with sizes, heights, shapes, and chemical environments that could be manipulated by the choice of molecular pillar. The layering motif would depend upon the sizes of the pillar and guest molecules that may occupy these voids. Sterically undemanding pillars and small guests would favor a bilayer motif, whereas large guests would favor a continuous single layer stacking motif. Large pillars would favor only single layer motifs with small guests or may even exclude guest molecules. The likelihood of these structures can be deduced from a simple geometric model that compares the area of a guest molecule, as projected onto the **GS** sheet, with the area available between the pillars in the different layering motifs.

We have this implemented this design strategy for the molecular pillars **I** to **VI** (**I** = dithionate; **II** = ethane-1,2-disulfonate; **III** = butane-1,4-disulfonate; **IV** = naphthalene-2,6-disulfonate; **V** = biphenyl-1,6-disulfonate; **VI** = naphthalene-1,5-disulfonate). Crystalline forms of these materials can be obtained readily by standard crystallization methods from methanol solutions, and in most cases crystallization occurs rapidly upon standing in the growth solutions. Pillars **I** to **III** form bilayer galleries in which planar **GS** sheets (θ_{IR} = 180°) are separated by the disulfonate pillars, which define 1D channels in the galleries. The channel width is established by the distance between sulfur atoms within a given **GS** sheet ($d_{ss} \approx 7.5$ Å), and the height of the channel is established by the length of the pillar. Pillar **I** is exceptional as its C_{3v} symmetry enables $(G)_2I$ to crystallize in the hexagonal space group $P6_3mc$, whereas the lower molecular symmetry of **II** and **III** forces a reduction of the lattice symmetry. The gallery thickness increases in the expected order $(G)_2I < (G)_2II < (G)_2III$. The pillared regions of $(G)_2I$ and $(G)_2II$ are devoid of guest or solvent molecules, but the greater void height in $(G)_2III$ accommodates two acetonitrile (CH_3CN) guest molecules in the lattice. The butyl residues exhibit the less favorable gauche conformation, apparently to optimize packing of the guest in the pillared layers.

G   I   II   III

IV   V   VI
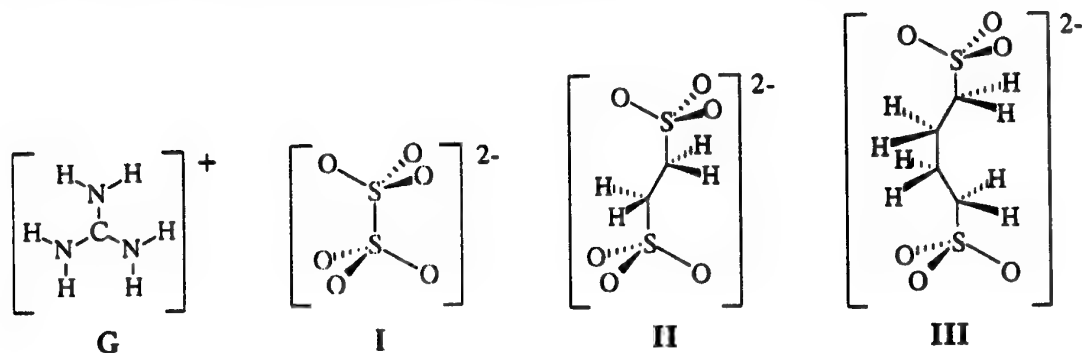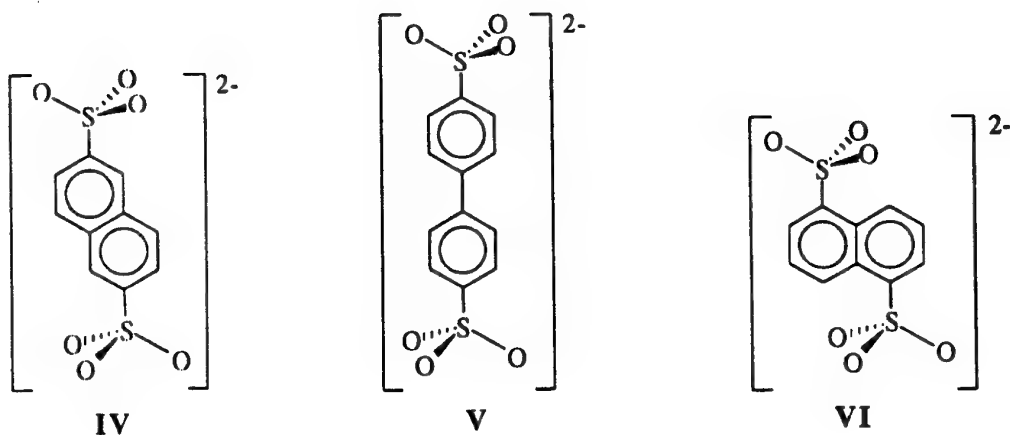
In the case of $(G)_2IV \cdot$benzonitrile, which crystallizes from methanol solutions containing benzonitrile, the naphthyl residues in the gallery form the walls of 1D channels oriented along a H-bonded ribbon direction of the quasihexagonal GS sheet. As expected from the axial length of IV, the gallery height is greater than that achieved with I to III. This enables inclusion of the larger benzonitrile guest molecules, which form 1D arrays parallel to the channel direction.

The system most extensively investigated by our group has been that based on the biphenyl-1,6-disulfonate pillar, V. Crystalline materials in which numerous aromatic guests, such as *m*-xylene, styrene, toluene, naphthalene, m-dibromobenzene, p-dichlorobenzene, p-methylbromobenzene, and 3-bromothiophene have been clathrated by this host lattice have been characterized by single crystal x-ray diffraction. These guests are enclathrated in the bilayer motif, in which the biphenyldisulfonate pillars form densely packed walls of 1D channels occupied by the guests. Small differences in the steric demands of these guests result in slightly different pillar tilt angles, which allows the 2-D networks to adjust to the vertical height of the guest so that void space can be minimized (that is, the gallery height changes according to the steric demands of the guest).
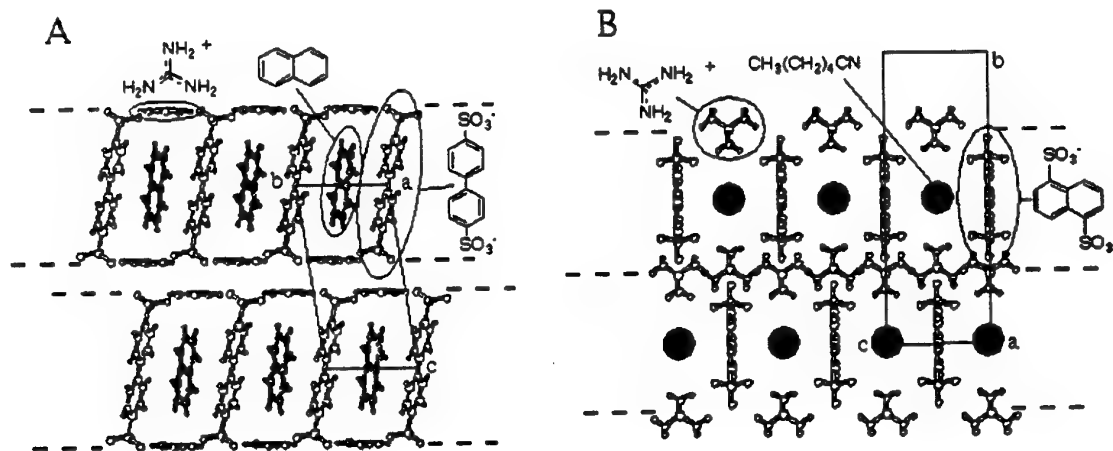

Figure 3. X-ray crystal packing diagrams of guanidinium organodisulfonate complexes. Guest molecules are shaded. (A) Guanidinium 4,4'-biphenyldisulfonate naphthalene complex (bilayer stacking). (B) Guanidinium 1,5-naphthalenedisulfonate 1-hexanenitrile complex (brick motif).

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The brick motif was first observed in our laboratory for the naphthalene-1,5-disulfonate pillar **VI**. These phases exhibit severely puckered quasihexagonal **GS** sheets in which the guanidinium-sulfonate ribbons actually are orthogonal to the channel direction. A consequence of this orthogonality, and the short span of the pillar, this phase exhibits one-dimensional channels with small cross sections. For example, $(G)_2VI\cdot2MeOH$ crystallizes from MeOH solutions as an orthorhombic phase with 1D occupied by MeOH guests. The channel walls consist of naphthalene pillars whose molecular planes are parallel to the channel direction, and the channel widths are established by the nominal distance between sulfur atoms in the quasihexagonal sheet (d_{ss} = 7.5 Å). Crystallization of $(G)_2VI$ phases from MeOH solutions containing linear substituted alkanes such as 1-alkanenitriles, α,ω-alkanedinitriles, 1-alkanols, and triglyme afford the same orthorhombic host lattice but with these guest molecules occupying the channels instead of MeOH. The $(G)_2VI$ lattice was highly selective for 1-alkanenitriles, with incorporation of $CH_3(CH_2)_5CN$ and $CH_3(CH_2)_4CN$ highly preferred among this class of guests. Although the topology of the $(G)_2VI$ host lattices is independent of the identity of the guest, θ_{IR} ranges from 34° to 89°. Because the channels are oriented perpendicular to the H-bonded ribbons, decreasing θ_{IR} values (increasing puckering about the interribbon (G)N-H⋯O(S) H-bonds) correspond to decreasing channel lattice constants. This suggests that the 1D channels can adapt to different guest lengths by network puckering, possibly driven by commensurism between the host and guest sublattices.

Recently we have observed the brick motif when the $(G)_2(V)$ host lattice is crystallized with either larger guest molecules or with molecules that are inclined to form aggregates in solution. The observation of these phases indicate that the guest molecules can be viewed as templates for the organization of the host lattice. For example, whereas crystallization in the presence of p-dichlorobenzene resulted in the formation of the bilayer motif, the slightly large guest p-dibromobenzene templates the formation of the brick motif. Similarly, divinylbenzene templates the formation of the brick motif whereas the bilayer motif is observed for styrene guests. Curiously, the brick motif was observed for nitrobenzene guests even though this molecule is small enough to fit in the voids of the bilayer motif. The nitrobenzene molecules are organized in the channel as double-decker stacks of anti-parallel nitrobenzene dimers, suggesting that crystallization was templated by nitrobenzene aggregates that are present in solution as a consequence of dipole-dipole interactions. The observation of these phases indicates that formation of the brick motif is possible, suggesting that rather large molecules can be enclathrated into this host lattice. This has interesting consequences with respect to generality in materials and process design based on these systems.

The synthesis of these nanoporous networks demonstrates that solid state motifs can be predictable if modules are used that can maintain their structural dimensionality and integrity with changes in ancillary functional groups. The use of the robust 2D **GS** networks reduces the crystal engineering problem to the last remaining dimension so that the pillar structure and nanopore dimensions can be adjusted rationally. The robustness of the **GS** networks can be attributed to their ability to adapt to the steric demands of different guest molecules without loss of the 2D architecture. The **GS** networks adapt by (i) puckering of the **GS** sheet about interribbon (G)N-H⋯O(S) H-bonded "hinges," (ii) switching between the quasihexagonal and shifted ribbon motifs, (iii) tilting of the pillars so that the network can shrink around the guest molecules, which is made possible by the flexibility of the (G)N-H⋯O(S) H-bonds, and (iv) adjusting the conformations of the pillars to optimize packing in the galleries. It also is important to note that the use of dense 2D H-bonded networks such as the **GS** sheets prevents network interpenetration that commonly frustrates the formation of voids in molecular crystals. These networks provide a platform for fundamental studies of solid state structure, and we anticipate that analogs in which the disulfonate pillars have specific functionality will have potential as host lattices for optoelectronics materials, molecular separations, and chemical reactions performed in the nanoscale voids.

5

Recognition of Convex Fullerene Molecules by Concave Complexing Agents. Structure and Reactivity.

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Introduction

Molecular recognition is mediated by a large variety of noncovalent interactions, including relatively strong metal-ligand bonds, electrostatic and donor-acceptor interactions, directional hydrogen bonds, anisotropic interactions between polarizable atoms and, also, relatively weak and isotropic van der Waals interactions. Mostly recognition is controlled by some combination of these and it is often difficult to assess their relative importance[1]. The role played by the weaker, isotropic interactions is best studied in the absence of the stronger, anisotropic ones. Fullerenes, aromatic hydrocarbons and their hybrids would seem ideal for studying weak interactions because they contain only hydrogen and sp^2-hybridized carbon atoms.

In order to achieve molecular recognition with weak interactions only, two factors require special attention. The recognition partners have to be of a certain size to ensure a sufficient number of intermolecular contacts, i.e. strong overall binding. In the absence of directional interactions, geometric shape and shape complementarity, i.e. close packing, are especially important[2]. Again, fullerenes, aromatic hydrocarbons and their hybrids are convenient objects for study, because they come in a range of sizes and in a variety of shapes.

Crystal packing

The study of molecular packing patterns in crystals is one approach towards understanding molecular recognition. Conversely, an understanding of recognition is useful for predicting crystal structures from molecular structures and from the conditions of crystallization, as well as for engineering the physical and chemical properties of crystals[1]. A study of polynuclear aromatic molecules in the crystalline state has revealed two important interactions[3]: (1) Weak electrostatic bonds between the small positive charges in the C-H perimeter of one molecule and the small negative charges in the carbon core of its neighbours[4]. These bonds are found between parallel molecules, which are shifted by various degrees relative to each other (~1.5 - 3.5 Å), and, more importantly, between molecules which are inclined to

each other (~50 - 90 deg). (2) van der Waals interactions between the carbon cores of stacks of parallel (but displaced) molecules. Although the details of the observed crystal structures are the result of a delicate balance between these interactions, the basic interaction types seem undisputed.

Planar vs. curved aromatic molecules

Most polynuclear aromatic molecules are more or less planar. In the presence of sterically congested fragments they become distinctly nonplanar. Examples include molecules containing the helical benzo[c]phenanthrene fragment or the decacyclene molecule[5] which can be described as a „monkey-saddle". Introducing five-membered rings into the aromatic nucleus leads to bowl-shaped molecules, e.g. the fullerene fragments $C_{20}H_{20}$ (corannulene)[6] or $C_{36}H_{12}$[7], and, eventually, to spherical fullerenes. For these molecules the atomic distribution in space can be described by curved surfaces, and characterized by a molecular curvature[8]. Surfaces with positive curvature are called convex, with negative curvature they are called concave.

Matching convex and concave surfaces is another element to be exploited in molecular recognition. It seems no coincidence that most weakly nonplanar aromatic molecules stack with a short translation distance between mean molecular planes ($<$ 4Å) and a small displacement parallel to them[3]. This ensures that shape complementarity is balanced against other interactions, $H(\delta+)...C(\delta-)$ in particular. Such a compromise is also seen in corannulene[6]. The two crystallographically independent molecules match parts of their complementary surfaces, but because of their bowl shape they are now rotated, rather than slided, with respect to each other to allow for some H...C interactions. In the case of $C_{36}H_{12}$[7], another molecular bowl, the molecules are nicely stacked by translation in spite of poor shape complementary: The curvature of the concave, inner surface is about three times as large as that of the convex, outer one. However, the rim of 12 C-H groups interacts with the cap formed by the 12 central carbon atoms of the next molecule. The shortest C-C distances are about 3.4 Å, the translational repeat is 5.2 Å, in the same range as found for stacked planar aromatics. The stacks of cups are polar and neighboring stack show the same direction of polarity. This can be understood in terms of their contact interface. Neighboring stacks have their surfaces inclined to each other in a way that is reminiscent of the inclination between stacks of planar hydrocarbons. This allows them to engage in the same type of H...C interactions. A combination of curved molecular surface and H...C interactions thus leads to a macroscopically polar crystal structure.

Fullerene cocrystals

Of the fullerenes, C_{60} it is the most difficult to pack because of its near spherical shape. The cubic and hexagonal close packings it assumes, contain octahedral and tetrahedral cavities with diameters of at least ~4 and ~2 Å, respectively. Not surprisingly, C_{60} forms cocrystals with a large number of solvents and other molecules. If crystallized from benzene, the basic cubic close packing pattern of C_{60} is maintained, but modified by deleting one out of every three rows of C_{60} molecules (along the [110]-direction). The channels which result give access to all of the cavities and most of the empty space is filled by benzene molecules, four per C_{60}[9]. The arrangement of the solvent molecules in the channels is reminiscent of the packing in the high pressure modification of benzene, but is about 25% less dense, and still about 5% less dense than in the ambient pressure modification. In any case, apart from filling space, the arrangement of the solvent seems to be controlled primarily by the typical benzene... benzene interactions[4]. If the benzene rings in the previous example are preorganized to some degree with the help of covalent bonds, molecular complexes may be expected. Calixarenes and related compounds form such complexes with C_{60}, both in the solid and in solution. Although not a pure hydrocarbon, we mention the example of a trimethyl-diiodocalix[5]arene[10]. Equilibrium constants for 1:1 association with C_{60} in benzene and toluene solution are found to be ~2000 at room temperature. In the solid C_{60} is embraced by two calixarenes, each of them displaying a bowl-shaped conformation.

An even higher degree of preorganisation is provided by the rigid corannulene molecule, which forms 1:1 cocrystals with both C_{60} and C_{70}. It contacts the fullerenes through its concave surface. In the case of C_{70}, corannulene has a choice to associate with the more curved polar or the less curved equatorial regions of the ellipsoidal C_{70} molecule. It chooses a location which is inbetween, but closer to the equator than the poles. This seems to allow for better H...C interactions.

Fullerene addition compounds

Several carbene and Diels-Alder addition products of C_{60} have been synthesized and characterized crystallographically. Many of these contain both convex and concave parts and are thus potentially self complementary. In bisanisylmethano derivatives of C_{60} the two anisyl groups form a mirror symmetric concave cleft which coordinates to the convex surface of a neighbouring methano fullerene[12]. Since 1,1-diphenyl

fragments prefer a chiral, twofold symmetric propeller conformation[13], the fit is induced and brought about by a rotation of the two phenyl groups by ~30 deg.

A more rigid and somewhat more open concave fragment is found in anthracene adducts of C_{60}. In the crystal structure of the monoadduct[14] the molecules are arranged in linear stacks, the intermolecular contacts being between the anthracene cleft and the spherical surface of the next molecule. In the bisadduct[15] with two anthracene fragments at opposite ends of C_{60}, the molecules form square, two-dimensional sheets. Each molecule recognizes two neighboring C_{60}-fragments through its anthracene groups and is being recognized by two anthracene fragments, one from each of two additional neighbors. Analogous patterns have been observed in cyclohexadiene mono- and tris-adducts of C_{60}[14,16]. Here the cyclohexene-fragments act as concave contact sites. The tris-adduct forms hexagonal sheets. Each molecule makes contacts to three neighbouring C_{60}-fragments through its cyclohexene fragments. Its C_{60} part is being contacted by the cyclohexene fragments of three other neighbours.

A thermal topochemical reaction

As mentioned above, the anthracene monoadduct forms linear stacks, ...C_{60} - $C_{14}H_{10}$... C_{60} - $C_{14}H_{10}$... . Heating to 180°C for a few minutes produces C_{60} and $H_{10}C_{14}$ - C_{60} - $C_{14}H_{10}$ in a one to one ratio and with ~96% conversion[14]. The driving force for this topochemical reaction is probably due to an increase in entropy, brought about by almost free rotation of C_{60} in the product crystal structure. The reaction can proceed through a sequence of thermally allowed cycloreversion - cycloaddition steps which are assisted by the parallel alignment of the dienophilic 6,6-bonds of the two C_{60}-fragments participating in the reaction. The high degree of conversion indicates cooperativity, the nature of which is not understood at present.

Conclusion

Analysis of crystal structures containing fullerenes, aromatic hydrocarbons and fullerene derivatives with aromatic substituents, suggests that weak interactions can mediate molecular recognition provided that their number is maximized by optimal shape complementarity. Some of the structures show interesting properties, e.g. macroscopic polarity or topochemical reactivity. These observations, although serendipitous, may serve as guidelines in crystal engineering.

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The Structure Of Solvates In The Solid State - Model Systems For Heteromolecular Association ?

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X-ray diffraction studies of crystalline solvates provide important information concerning the possible structural modes of heteromolecular association. Whether this information is of more general importance, i.e. not limited just to the solid phase, is an interesting question [1]. The purpose of the present paper is twofold. It is to deliver some recent structural data on solvate architecture and physicochemical behaviour and to be an introduction to the panel discussion which may, hopefully, answer the title question. The data are selected from recent studies performed jointly with the Novosibirsk and Kishinev groups, and refer to hydration of crown ethers and their molecular complexes, and to solvation of coordination complexes by organic solvents.

In the crystal structures of crown hydrates two different modes of hydration co-exist. These are: *hydrophilic hydration*, in which water is H-bonded to its counterpart, and *hydrophobic hydration* in which water molecules *enclathrate* lipophilic parts of the second component. Recent results of x-ray diffraction studies on, mostly yet unpublished, binary crown-water and ternary crown-guest-water crystalline compounds will be given. As the example of hydrophilic hydration complexes of 18-crown-6, its monoaza and 1,10-diazaderivatives, and dicyclohexylo-18-crown-6 (host) with silicon tetrafluoride, pentafluorosilicate [2], boron trifluoride and tetrafluoroborate with different amount of water [3] will be discussed. Hydrophobic hydration of a variety of organic ammonium salts by 18-crown-6 will be presented: methylammonium halogenates (F^-, Cl^-, Br^-) [4], ethylammonium fluoride [5],

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ethylenediammine dichloride, and 1,3-propylenediamine and 1,4-butylenediammine difluorides [6]. Fascinating variety of structures have been found. Water molecules aggregate to form two-dimensional layers incorporating halogen anions, or expanding in its regions into third dimension [7]. The formation of channel structure in which fluoride anions are loosely accommodated inside the channels formed by water molecules has also been found. Crown molecules, when complexed by ammonium cation or aminoacid terminal $-NH_3^+$ group, do not form hydrogen bonds to the water molecules. Instead, on hydration of pure crowns or their silicon or boron fluoride complexes, rather extensive hydrogen bonding water-crown is observed. The hydronium H_3O^+ ions, when present in the crystal structure, compete with the Lewis acid moieties in complexation to the crown macrocycle through hydrogen bonding. This gives rise to two different patterns of guest-macrocycle hydrogen bonds in which, respectively, water molecules mediate the crown-substrate bonding and form polymer-like chains -crown-substrate-water-substrate-crown- .
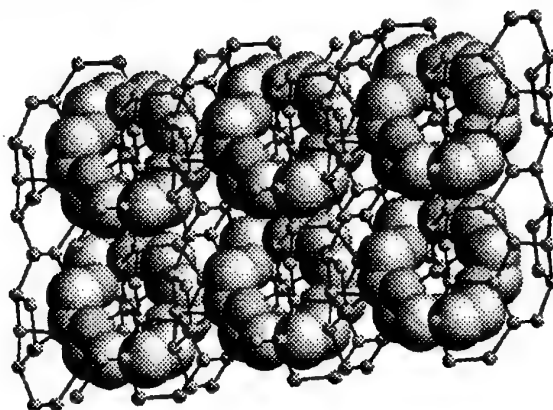
The structure of 18-crown-6 dodecahydrate.

Novel structural information on hydration pattern found in complexes: 15-crown-5 octahydrate, 18-crown-6 hexahydrate, and dodeca-hydrate and its ternary complex with glycine (1:1) and water (3:1), 1,10-diaaza-18-crown-6 monohydrate, dihydrate and nonahydrate and its ternary complex with gly-gly-gly and water (1:1:5) [8] will be given, discussed in terms of their thermodynamic characteristics, and compared to hydration of alkylammonium salts.

Some coordination complexes show remarkable tendency to co-crystallize with foreign molecules (often crystallization solvent as the most easily

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available species) thus forming a variety of inclusion compounds [9]. A suitable example is the series represented by the general formula $M^{II}X_2A_4$, where M stands for a divalent metal cation, X - monovalent anionic and A - monodentate neutral ligand. The complexes display outstanding ability to form broad range of inclusion - type compounds. Their crystal structures depend upon the guest, its content in the solid, and upon thermodynamic conditions of preparation. In several cases more than just one crystalline phase is formed in the system under investigation, depending on external physicochemical parameters. E.g. the $Cu(NCS)_2$(4-methylpyridine)$_4$ complex, when crystallized from 4-methylpyridine below 5° C, forms blue crystals containing 2 moles of included solvent per mole of the complex but the crystals quickly transform into green solid of the composition 2/3 : 1 when heated above that temperature [10].
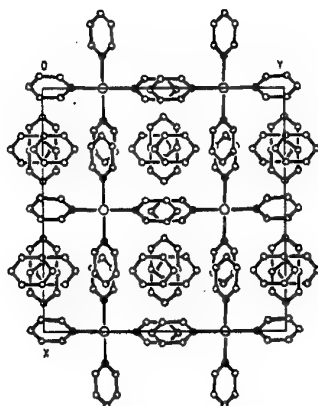

Figure: Example of an inclusion compound formed by the NiX_2py_4 complex

In the present paper recent x-ray structural data on several inclusion - type compounds of the type mentioned above will be discussed together with their physicochemical characteristics [11 12 13 14 15]. In particular, special emphasis will

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be put on the non-stoichiometric behaviour of the, so-called, *organic zeolites* formed by coordination complexes. In contrast to the most of the literature data available, in the structures under investigation, guest content may go beyond the maximum sorption capacity (to a small extent). The resulting *overloaded structure* may be considered as the precursor state for formation of another phase, in which guest sorption capacity is higher (e.g. layered type) [16].

Several recently obtained experimental data will be discussed in order to demonstrate that formation of solvates of the inclusion - type structure is rather common phenomenon in coordination chemistry. Several solvate structures reported in the literature are actually inclusion type compounds in which extra ligand molecules are located in the intermolecular spaces left empty by the host complex. Thus, inclusion-type solid solvates appear as rather common solid state phases, not being limited to some special host material. Virtually, any coordination complexes may, in suitable conditions, be prepared in a form of a solvate, inclusion compound, or clathrate. This allows chemists to investigate structural behaviour of coordination complexes in different chemical environments, thus giving a new dimension to the crystallography of that class of chemical compounds. Distortion isomers and unstable conformers may be investigated by x-ray diffraction in the solid state. It leads to the concept of *contact stabilization* of molecules (Dyadin).

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Supramolecular Architectures and Hydrogen Bonding in Organometallic Crystals

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Crystal engineering conforms strictly to the paradigm of supramolecular chemistry, i.e. the intelligent utilization of non-covalent interactions to make aggregates that function differently from the individual components. Since materials chemistry is concerned with the function of solids, crystal engineering can be viewed as a bridge between supramolecular and materials chemistry.

The use of organometallic molecules or ions in the construction of crystals with predefined architectures is a means to bring in the supermolecule-crystal the variable oxidation and spin states of metal atoms as well as the specific topological requirements of coordination bonds.

The effect of ligand topology, the ability of tuning the acid/base behavior of ligands by means of ligand-metal(s) coordination, the direct participation of metal atoms in extramolecular interactions in the solid state, as well as the consequence of the ionic charges on the strength of weak and strong intermolecular hydroegn bonds will be discussed. In particular, a design strategy to obtain organic-organometallic supramolecular aggregates in the solid state by means of a selective use of strong hydrogen bonds between the organic component and of weak hydrogen bonds between organic and organometallic components will be illustrated with emphasis on the role of charge assisted $C-H^+ ... O^-$ hydrogen bonds.

The perspectives of an organometallic crystal engineering discipline, within the frame of supramolecular chemistry will be discussed.

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WEAK HYDROGEN BONDS IN SUPRAMOLECULAR SYNTHESIS

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The weak hydrogen bond, typified by the $C-H...O$ interaction, has found much use in the assembly of supramolecular crystalline architectures. At the outset, it must be emphasised that the term 'hydrogen bond' is applied to this interaction because it has many of the attributes and characteristics of the strong hydrogen bond, such as dependence on the acidity and basicity of donor and acceptor groups and cooperative properties that enhance interaction strength. The fall-off of interaction effectiveness is much more gradual for weak hydrogen bonds than it is for van der Waals interactions and hence these situations need not be confused with each other. Even as the shrinking grey area between the weak hydrogen bond and the van der Waals interaction is particularly contentious, it appears that there is a structural continuum between these limiting possibilities.

In this talk, some recent examples of crystal engineering with weak hydrogen bonds will be presented.

Molecular Networks : Design, Synthesis and Structural Analysis of Coordination Polymers in the solid State

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Because transition metals offer numerous oxidation states, coordination geometry as well as photochemical and magnetic properties, the design and preparation of coordination polymers, which may be regarded as metallo-organic networks, are topics of current interest.[1]

Using the molecular tectonics approach dealing with the self-assembly of complementary molecular tectons,[2] we have prepared in the solid state molecular networks based on weak van de3 Waals interactions employed to include convex connectors into concave receptors,[2] or on combination of electrostatic and hydrogen bonding.[4] A further step in our strategy would be the use of coordination bonds for assembling metals and organic ligands into molecular networks.

One may control the overall topology of coordination polymers by the coordination preferences of the linking metal as well as by the topology of the bridging ligand. Thus, using metal cations adopting tetrahedral coordination geometry and bis-bidentate exo-ligands, one may envisage the formation of either discrete cyclic or infinite linear polynuclear species. Depending on the geometrical features of the ligand, a selection may be induced between the different possibilities. Indeed, with bis-bidentate exo-ligands adopting a planar conformation only 1-D linear coordination polymers may be envisaged (Figure 1a). On the other hand, with non planar bis-bidentate exo-ligands adopting a "roof-shaped" conformation, in addition to discrete cyclic polynuclear species such as the tetranuclear complex presented in figure 1b, infinite 1-D networks of the "stair type" (Figure 1 c) or single stranded helical species (Figure 1d) may be formed. However, by imposing constraints such as steric hindrance, one may favour one of the alternative structures.
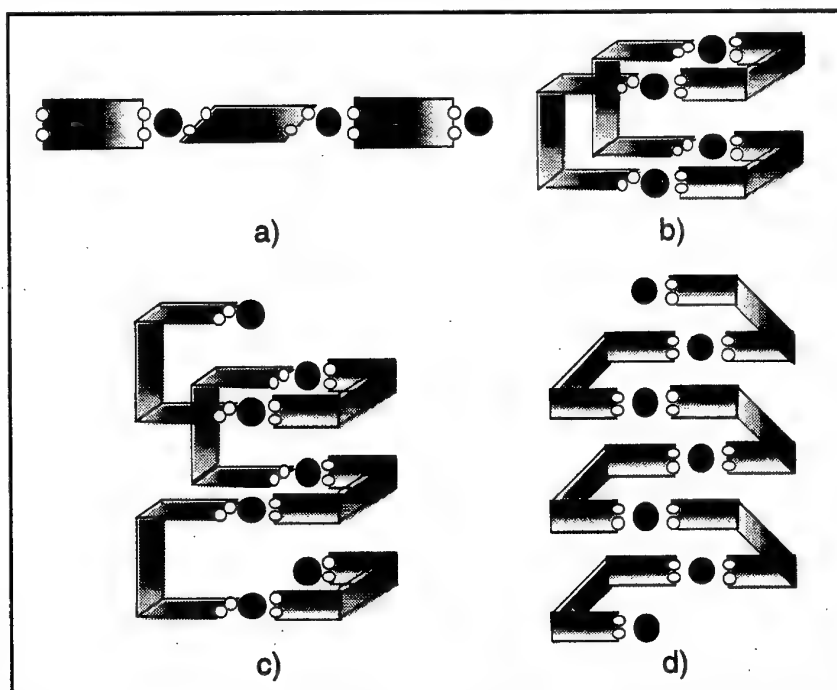
Figure 1 : *Schematic representation of different types of arrangements that may be obtained by self-assembly of exo-ditopic ligands and tetrahedrally coordinated metal cations: a) linear, c) "stair type", d) helical coordination polymer and b) discrete tetranuclear species.*

In order to impose a restricted conformational space and to control both the distance and the localisation of metal centres, one may use exo-ligands based on macrocyclic frameworks.[5-7] In particular, exo-ligands **1-7**, resulting from the interconnection of two 2,2'-bipyridine units at the 4 and 4' positions by different spacers were prepared.[7]

Figure 2

Using compound **7** and silver cation a helical coordination polymer was formed. In the solid state, the structure of the molecular assembly was elucidated by an X-ray analysis[8] which revealed that the cationic component of the structure was indeed a single stranded helical network formed by mutual bridging of silver atoms and ligand **7** (Figure 3). The pitch of the single helix was composed of four Ag atoms an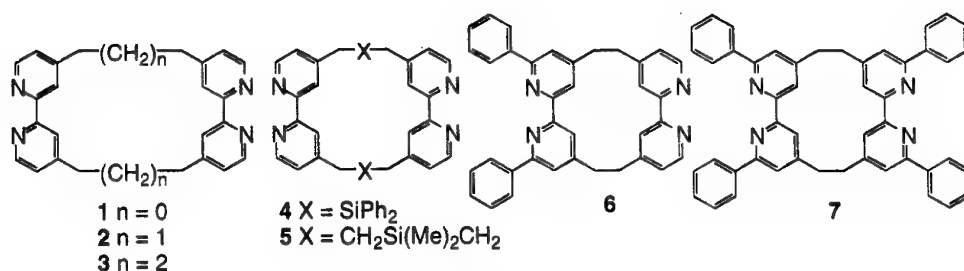d four ligands. The interior of the helix was obviously not empty but occupied by phenyl groups . The interstices in the solid were occupied to different degrees of intrusiveness by CH_3CN molecules and PF_6^- anions.
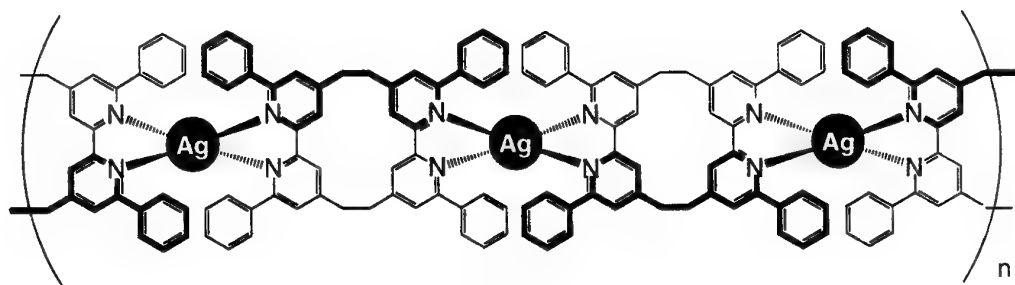

Figure 3

The observed helical structure was derived from the primary structure of the ligand **7** adopting a "roof-shaped" conformation in the complex. However, since by design, no intrinsic chirality was coded within the structure of the connecting ligand, a racemic mixture of both the right- and left-handed helical coordination polymers was expected and observed.

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COMPUTER SMULATIONS ON COMPLEX SYSTEMS: IONS AND IONOPHORES AT THE LIQUID -LIQUID INTERFACE

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Despite the many studies devoted to liquid-liquid extraction of ions by ionophores, surprisingly little attention has been paied so far to the interfacial behaviour of these species. We describe a number of computer MD simulations on the water - chloroform interface, with ionophoric ligands L free or complexed (L = crown ethers, cryptands, calixarenes, CMPO, TPTZ, TBP, podants ...). It is found that the ionophores, although more soluble in the organic phase than in water, display a strong affinity for the interface. Lipophilic anions commonly used in extraction experiments, like Picrate, are also found to strongly adsorb. These conclusions, consistent with related macroscopic data, are confirmed by the calculation of the free energy profiles for crossing the interface.

Other computer experiments presented concern (i) the formation of monolayers at the interface with L, LM^{n+} or $LM^{n+}.X^-$ complexes, (ii) the question of water content and structure in the organic phase, and (iii) the demixion of a "vigourously shaken" water - chloroform solution containing ionophoric solutes. Based on the simulations, a mechanism for assisted ion trnasfer is proposed.
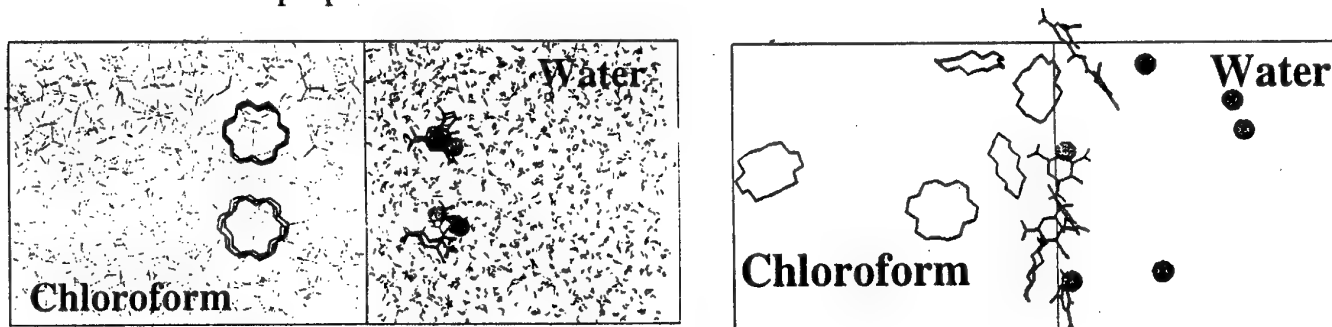
Left: MD simulation starting with six *18C6* molecules in chloroform, and six K^+ *Pic⁻* ions in water . Right: final situation after 1 ns (solvent not shown).

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Self-organization of organic molecules in crystals, liquids and solutions.
Static and dynamic calculations

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The study of intermolecular interactions in molecular systems has seen great advancements in the last decades, thanks to the detailed structural information made available by X-ray diffraction studies in crystals. Although recognition and systematization of existing structures has provided a number of clues on the basic mechanisms of molecular recognition that lead to the formation of condensed phases, theories are still in a rudimentary stage.

A basic accomplishment for the chemically oriented crystallographer would be to provide an answer to questions such as the following ones, given only molecular constitution and connectivity: will this molecule crystallize at all, in a reasonable temperature range? what will be the external appearance of the crystal crop? what would be best - growth from solution, from melt, from vapor? are polymorphs possible for this compound? will this molecule form clathrates or inclusion complexes, and with what guest molecules? can one guess the density and sublimation enthalpy? are there any key recognition locking points, and can one expect some partial packing motifs - rings, chains, layers, herringbones? can unique cell dimensions and space group be predicted? can the molecular conformation, as well as the location and orientation of the molecule within the cell, be predicted with good accuracy? And ultimately: can one steer the answers to all of the above questions by changing in a rational and systematic way the chemistry of the molecule?

Static computer simulations (that is, using empirical formulations for the potential, but neglecting the effects of kinetic energy) can provide estimates of heats of sublimation, of enthalpy differences between polymorphs, and of lattice vibrational frequencies and entropies. The crystal structure can be guessed, with moderate success, by recursive crystal construction algorithms; examples of the above will be discussed.

On a more fundamental level, however, understanding and predicting crystal structures requires also control of their liquid - melt or soluton - precursors. One is therefore brought to a consideration of the complete phase behaviour of an organic molecule, and, for any liquid state, static calculations are clearly inadequate. In principle, molecular dynamics simulations allow the study of all stages of recognition and condensation, in terms of structure, thermodynamics and kinetics. There are however, as could have been anticipated, quite a few stumbling points, some of which are summarized below:

1) the force field problem: parameterization of a force field for dynamic simulations is even more problematic than for static lattice energy calculations;

2) polarisation: especially for solvent-solute interactions, mutual polarisation is presumably one of the main driving forces in the dynamical evolution, but no simple and sound method for empirically accounting for polarisation is apparently available;

3) the problem of a robust and reproducible sampling of phase space;

4) the timescale problem: even on the fastest available computers, simulation times on chemically significant systems (10,000 atoms) are limited to the order of nanoseconds, adequate for the lattice dynamics and for diffusion in a liquid phase, but presumably too short by orders of magnitude for nucleation, for growth of elementary nuclei, for phase transitions among solids, for freezing and ordering in molecular clusters, and for melting;

5) the design-interpretation problem: computational chemistry requires the design of an appropriate computational experiment, and a sound and skeptical interpretation of its results, otherwise one is just piling up an inordinate amount of uninterpretable numerical data.

Consider a chemical system consisting of a number of different molecular species, Ai, each molecule with an unperturbed potential field Ui* and at infinite distance from any other molecule. As the volume of the system is reduced, molecules begin to interact, and polarization distorts the molecular fields from Ui* to Ui. Under the action of the fields, molecules are driven together to aggregate, against random diffusion motions; a cluster is defined as an ensemble of molecules whose centers of mass librate around an equilibrium position, and which are in a collective potential energy valley (as distinct from a saddle point), that is, no thermal libration may disrupt the ensemble without expense of energy: as such, the cluster has a recognizable pseudo-crystalline structure. We define molecular recognition as one elementary step in the addition of one molecule to an already existing cluster; therefore, in a perfect, ordered crystal, paradoxycally, according to some different definitions, molecular recognition no longer occurs.

If interactions with the medium are neglected in a first approximation, nucleation of an organic compound from solution involves only one molecular species, A, and molecular recognition is (square brackets denote a cluster):

$$[nA] + A \rightarrow (n+1)A] \qquad (1)$$

with n going from 1 to a few units or a few tens. The thermodynamics and kinetics of recognition are in principle different for each step, since the structure and potential of the cluster depend on n. Crystal growth may be described by this equation with n very large, and slowly approaching Avogadro's number. Even in the ultimate stages, when the crystal has already taken macroscopic dimensions, growth is likely to proceed by addition of single molecules, rather than by sintering of clusters of different sizes.

Moreover, clusters may be structurally flexible: that is, rearrangement steps may occur:

$$[nA]j \rightarrow [nA]k \qquad (2)$$

where the index denotes a conformation, or a particular arrangement of molecules within the cluster. In the nucleation stage, the number of these arrangements must be small, otherwise one runs into the fluxional clusters proper of the liquid state; in the growth stage, n is very large, and equation 2 represents the migration of the last incoming molecule through the surfaces, steps and kinks of the nucleus, on its way to its proper location.

The enthalpy of addition can be approximated as:

$$\Delta H+ = E[(n+1)A] - E[nA] - E(A) \qquad (3)$$

while the rearrangement enthalpy can be estimated as the difference in energy between the two conformations of the cluster:

$$\Delta H(jk) = E[nA]k - E[nA]j \qquad (4)$$

Both enthalpy differences could be calculated using empirical potential fields, if the structures of the clusters were known. But even in this very favorable and unlikely case, confidence in the results would be limited by the lack of polarisation in the force field formulation. Besides,

clusters have a finite size and well defined boundaries, and therefore contributions from surface effects should be included for a proper treatment. But, unfortunately, no simple methods are available for their computational estimation.

The theoretical study and the computer simulation of all the above may proceed through molecular dynamics. Examples will be given for the nucleation of acetic acid from carbon tetrachloride. Problems, possible remedies, as well as promising computational experiments, will be reviewed.

Nucleation for crystallization from the melt could be described by the equilibrium:

$$(m+n)A \;=\; [mA] + nA \tag{5}$$

with m+n of the order of Avogadro's number, and m of the order of a few units to a few tens. The microscopic cluster [mA] swimming in the bulk liquid nA could evolve and grow by a coupling of the following two steps:

$$[mA]j \;\rightarrow\; [mA]k \quad \text{and} \quad [mA] + A \;\rightarrow\; [(m+1)A] \tag{6}$$
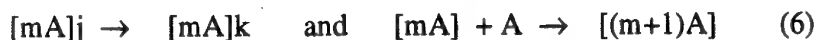
Melting could be described as the collapse of the macroscopic cluster [(m+n)A] representing the crystal structure. Premelting phenomena, or rearrangements and transitions within the crystal structure that preserve long- range order, could be symbolized as

$$[(m+n)A]j \;\rightarrow\; [(m+n)A]k \tag{7}$$

Actual melting is almost certainly preceded by some local loss of order, of which surface melting is the most likely form. This would split the crystal in two regions, one still crystalline and one liquid-like, the former merging eventually into the second.

The computational study of the solid-liquid equilibrium can in principle be done by MD. The timescale problem is, in this case, devastating. A relatively large number of simulations have been carried out on the Lennard-Jones system, or an ensemble of, typically, a few thousands of spheres interacting via a 12-6 potential - a sort of computational Guinea pig. Examples, possible applications to actual organic molecular systems, computational experiments, and future developments will be reviewed.

TIME-RESOLVED STUDIES OF CLATHRATE HYDRATE FORMATION

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The simple (two-component) clathrate hydrates are probably the best understood examples of templated, self-assembled lattices. About 150 guests are known to form either the cubic structure I or structure II clathrates[1,2]. Each hydrate family has unit cell parameters that are very similar, and has compositions that are variable but within well-known limits. Recent interest in hydrates has been sparked by the vast quantities of natural gas stored in off-shore hydrate deposits that exist in many locations on the continental slopes[3].

Over the years there has been much interest in the processes by which hydrates form: a solid lattice is assembled from liquid water and a gaseous guest that is often quite insoluble in water[4]. Alternatively, hydrates will form directly from solid ice and gaseous guest. It is also of great technical interest to learn how to prevent hydrates from forming, as solid hydrate plugs are known to form in pipelines used for the transmission of gas and crude oil, often with disastrous results[5]. Today, much effort has been expended on so-called kinetic inhibitors that slow the growth of hydrate crystals after nucleation. Thus, the study of processes such as nucleation, crystal growth and inhibition of crystal growth, from a molecular point of view, are of critical importance.

Over the years we have used 129Xe NMR spectroscopy as a technique to study structural aspects of the clathrate hydrates[6]. In fact, this technique played a large part in identifying a new structure known as structure H hydrate[7]. Briefly, each guest site, commonly known as a hydrate "cage", gives a xenon guest in that cage its own spectral signature that reflects both the cage size and the cage symmetry. However, it has been difficult to use 129Xe NMR spectroscopy as a technique to study processes because of the long times usually required for data collection. This is due to the low inherent sensitvity of the NMR technique and the long relaxation times of the xenon atom inside the hydrate cages.

The recent development of NMR spectroscopy with hyperpolarized noble gases has increased the sensitivity of the NMR experiment by a factor of up to ~ 104 [8]. Hyperpolarized xenon can be produced by optically polarizing Rb vapour by laser pumping in a magnetic field and transferring the polarization to xenon atoms through a transient binary complex that exists in the gas phase. The hyperpolarized state persists long enough so that the xenon can be transferred to appropriate samples for observation by NMR spectroscopy.

We have followed the formation of clathrate hydrates on the surface of powdered ice with hyperpolarized xenon. Time resolution down to ~ 40 msec can be achieved with excellent signal to noise ratios thus allowing the observation of site-specific kinetic processes. We have observed that rapid hydrate formation is preceded by an induction period. This has been observed previously in macroscopic kinetic experiments using gas up-take measurements[4]. By measuring the site occupancy as a function of time, it can be seen that during the induction period the composition of the material changes rapidly, and that only after the composition has reached its equilibrium value rapid hydrate growth commences. The induction period can be identified with the time required for surface adsorption, cluster building and nucleation. The composition data taken at the earliest times point toward a specific hydrate precursor state. The induction period varies systematically with temperature and pressure, thus identifying the driving force for nucleation. The induction period disappears if the surface is re-exposed to xenon after the hydrate layer is destroyed be desorption. This suggests the presence of a structural memory effect at the surface.

Some initial experiments with polymer inhibitors suggest that sorption with hyperpolarized xenon may be one way of learning about the mechanism of growth inhibition.

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DIRECT PHASING METHODS FOR LARGE MOLECULES.

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Structure analysis by X-ray crystallography permits the positions of atoms within a crystal, and thus the shapes of the component molecules, to be determined. The atomic positions are related to the amplitudes and relative phases of the X-rays diffracted by a crystal, but only the amplitudes can be measured experimentally. Direct phasing methods utilize probabilistic relationships among certain linear combinations of phases to supply the missing phase values. The so-called reciprocal-space representation of a structure (amplitudes and phases) can be converted to the real-space representation (atomic coordinates) via Fourier transformation.

Shake-and-Bake is a state-of-the-art algorithm for the direct phasing of single-crystal diffraction data. This procedure extends the range of successful applications of conventional direct methods from approximately 100 independent non-H atoms to small proteins containing over 1000 atoms. The improvement made possible by Shake-and-Bake depends largely on unconditional cyclic alternation of reciprocal-space phase refinement with filtering in real space to impose physically-meaningful constraints. As implemented in the computer program SnB, Shake-and-Bake employs a multi-trial approach in which (i) initial trial structures consist of randomly positioned atoms, (ii) phase refinement is based on either the Karle-Hauptman tangent formula or parameter-shift optimization, and (iii) density modification in the form of peak picking is used in real space. Choosing appropriate values for the control parameters (such as the number of phase relationships used during refinement or the number of peaks in the trial structures), selecting the optimum phase-refinement method, and performing an adequate number of refinement cycles are critical for successful large-molecule applications. Success is also strongly dependent on the quality of the diffraction data (both accuracy and completeness) and on the complexity of the structure.

The dual-space Shake-and-Bake procedure, like traditional direct-method protocols, typically fails at resolutions below 1.1-1.2Å. However, some structures, including vancomycin and an interesting peptide crystallizing in space group I4, can be solved by SnB at 1.4Å. These 250-300 atom structures contain eight chlorines and ten sulfurs, respectively, and it seems likely that the presence of these "heavier" atoms facilitates solution at lower-than-normal resolutions. The SnB development team is currently investigating ways of using additional information (e.g.,

from three-beam or anomalous dispersion experiments) to strengthen the direct-phasing process and routinely extend its resolution range. The largest structures having only first-row elements which have been solved so far have contained about 300 non-H atoms.

Detailed information concerning the SnB program is available at the Web site http://www.hwi.buffalo.edu/SnB. Since SnB is user-friendly and efficient default parameter values are supplied, it is suitable for use as a "black box" by noncrystallographers. A review of the Shake-and-Bake method can be found at http://www.sdsc.edu/Xtal/IUCr/CC/School96.

BOTTOM UP FABRICATION OF SUPRAMOLECULAR ASSEMBLIES AT SURFACES USING SCANNING PROBE METHODS

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An ultimate aim of fabrication is the controlled positioning of atoms and molecules into perfect functional structures. Here we present different Strategies and Approaches towards this goal and using specially developed modes of scanning probe microscopy. In combination with self assembly and growth, we describe the creation of two and three dimensional molecular structures at solid surfaces.

EXPERIMENTAL ELECTRON DENSITIES
THEIR USE IN THE CALCULATION OF INTERMOLECULAR INTERACTIONS
AND THE PROSPECTS FOR THE MEASUREMENT OF TRANSIENT LIGHT-INDUCED CHANGES IN THE ELECTRON DENSITY

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1. Introduction

This lecture will cover two advances in crystallographic techniques that are relevant to the field of Supramolecular Chemistry. They are:

a) the mapping of charge densities in crystals, and the resulting ability to probe electronic structure and calculate intermolecular interactions using parameters appropriate for the molecular environment in the crystal, and

b) Time-resolved studies of photoinduced changes in molecular crystals, a field that has the considerable potential for elucidation of the structure of transient species in chemical processes.

2. The Measurement of Charge Densities by X-ray Diffraction

2.1 Background

The ability to measure the experimental charge distribution in crystals from the intensities of the scattered X-rays was realized almost immediately after the discovery of X-ray diffraction. The goal became within reach as a result of technical developments that occurred in the 1960's and 70's, including new diffractometer designs, automation of data collection, much better low temperature techniques and advances in computing power and specialized software. In the last few years this data collection has been further revolutionized by the advent of area detectors, which rapidly provide large amounts of quite accurate intensity data, and by the development of the program system XD for Charge Density Analysis.

The experimentally obtained electron distribution can be compared directly with theoretical results, and can be used to derive other physical properties, such as electrostatic moments, the electrostatic potential and lattice energies. Coulombic interactions between non-overlapping charge distributions can be directly derived from the diffraction results, and the effect of the molecular environment on the charge distribution can be analyzed.

2.2 Methods

Among the tools currently used in X-ray Charge Density Analysis are:

a) The aspherical atom scattering formalism. Once a set of accurate structure factors are available and the basic structure has been determined, the structure factors are analyzed in terms of an aspherical atom formalism, in which each atomic density is represented by a spherical harmonic expansion of density functions, each with its specific population coefficient. The density functions are directly related to the atomic charges, atomic dipole- and higher moments.

b) Topological analysis of the total density. The topological analysis of the total density according to the aspherical atom formalism, following the *Atoms In Molecules* method of Bader[1] has become a general tool, as it allows quantification of the bonding between atoms and direct comparison between experimental and theoretical results.

c) Derivation of electrostatic properties. The electrostatic moments and the electrostatic potential of a molecule in the crystal can be derived directly from the results of the aspherical-atom refinement of the diffraction data. The electrostatic interactions between non-overlapping charge distributions can be expressed in terms of the atomic multipoles, using well-known expressions.

d) Analysis of the occupancy of transition-metal d-orbitals. For transition metal atoms the populations of the spherical harmonic functions can be converted into d-orbital occupancies, using a matrix transformation.

A detailed description of the methods and a summary of results can be found in ref [2]

2.3 Application to non-covalent interactions

Electrostatic interactions are of prime importance in intermolecular closed-shell interactions. A reliable calculation requires the incorporation of multipolar interactions. For many molecular crystals electrostatic interactions contribute 50% or more of the interaction energy, and the same will be the case for many supramolecular assemblies. Analysis of the dependence of the charge distribution on molecular conformation and molecular environment is one of the frontiers of the field.

3.0 Photoinduced changes in crystals and the study of transient species

3.1 Background

Photochemical reactions in crystals have been an active area of research since the pioneering studies of Schmidt and coworkers, who showed that the nature of the products of a solid reaction is topochemically-controlled by the geometry of the crystal structure.[3]. Advances since that time have put at our disposal highly intense pulsed synchrotron sources, pulsed lasers, fiber optic light guides, cryostats, helium gas-flow systems and area detectors. We have exploited the new technology in low temperature diffraction studies of long-lived metastable states of transition metal nitrosyl complexes.[4] A powerful further extension concerns stroboscopic experiments on transient species with lifetimes of ms and less.[5]

3.2 Experimental Strategy

By suitable synchronization of the laser and synchrotron pulses an instantaneous non-equilibrium concentration is established and probed before significant decay occurs. Such experiments have now been performed to study processes such as the photodissociation and recombination of myoglobin and carbon monoxide.[6],[7] In these experiments the polychromatic Laue technique is used with a single synchrotron bunch of 60 ps length. By varying the delay between the exciting pump pulse and the probe pulse, the reversible dynamic process can be followed on a very fine time scale, and a "motion picture" of the reaction can be obtained. For experiments that aim at detailed atomic resolution or better, monochromatic methods must be employed in a stroboscopic experiment on a reversible process, in which diffraction intensities are accumulated over a number of synchrotron photon pulses.

For such experiments to be successful, the number of photons in the exciting laser pulse must be of the same order of magnitude as the number of molecules in the crystal. This is well within reach of current technology. A 5 kHz Nd-YAG laser with a 50mJ pulse energy gives, for example, about 10^{14} photons per pulse at 355nm. For a typical complex, 10^{14} molecules corresponds to a 40 x 40 x 40μ crystal, which is what is used in many synchrotron diffraction experiments. Working with small sample crystals has the further advantage that illumination is more uniform, and heat dissipation to the surrounding is enhanced. A reasonably uniform illumination requires that only a fraction of the incident beam is absorbed, so that not all photons will lead to excitation. To counter this effect, the number of active molecules can be reduced further by embedding the molecules as hosts in a spectroscopically

inert matrix. The advantages are that i) the number of molecules to be excited to obtain a given conversion percentage is reduced, ii) concentration quenching due to exciton–exciton annihilation will be diminished, and iii) choice of a transparent host will increase the transparency of the solid to the exciting light, and thus assure more uniform illumination.

Possible host systems are microporous inorganic solids such as zeolites and aluminophosphates, which are known to incorporate organic guests including p-nitroaniline (p-aminonitro phenyl),[8] organic hosts such as b-cyclodextrin, for which detailed photochemical experiments show enhanced luminescence upon complexation,[9] as well as organic framework structures as formed, for example, by bis-(2.5 resorcino:) 9.10 anthracene.[10] In other words, Supramolecular Chemistry is highly relevant for such studies.

3.2 Selected applications

a) Transition metal complexes

Examples of transition metal complexes with photoinduced excited triplet states having ms lifetimes are the binuclear metal d^8-d^8 complexes of rhodium and platinum. They show unusually reactivity, and are, in solution, intermediates in metal-catalyzed photoreactions of small molecules and organic substrates.[11] Since for d^8-d^8 complexes the excitation corresponds to a ds* Z ps transition, very large contractions of the metal-metal distance occur if the bridging ligands are sufficiently flexible. An example is $Rh_2(dimen)_4^{2+}$ (dimen = 1,8-diisocyanomenthane) for which metal-metal bond shortening from 4.8 E to E3.2 E upon excitation to a 21 ms lifetime state has been deduced from spectroscopic information. On the other hand, single metal-metal bond Rh^0_2 and Rh^0Rh^{II} complexes with the bridging ligand (difluorophosphine)methylamine, $(PF_2CH_3N(PF_2)$, undergo excitation into a ds* orbital, and are expected to show bond lengthening upon excitation.[12] In none of these cases is the distortion of the ligands and the change in metal-ligand bond distances upon excitation known.

b) Photo induced electron transfer and charge-separated states

The electronic response of systems at the molecular level has been one of the most active areas of research in recent years. Electron transfer within a single molecule with donor, bridging and acceptor groups, is of importance for energy conversion and the storage of information,[13,14] and has been proposed for the design of molecular computing devices.[15] Synthetic triad and tetrad molecules, containing for example a carotenoid donor, porphyrin or metal-

porphyrin bridge and quinone acceptor(s) are being studied extensively for such purposes.[16] Information on geometry changes along the reaction path of the photochemical charge separation and recombination is presently lacking, but would be important for our understanding of photochemical processes.

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TIME RESOLVED X-RAY DIFFRACTION IN CRYSTALS AND LIQUIDS

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In this lecture our novel experimental system used for time resolved x-ray experiments will be described. The data obtained will be compared to the results calculated using the kinematical theory for x-ray diffraction and show that there is a very good agreement between theory and experiment.

The experimental system which we utilized to generate picosecond x-ray pulses is a photo activated x-ray diode consisting of a metal anode and a photocathode which is activated by picosecond UV pulses.

The x-ray diode is driven by 0.5 to 2 ps , 193 nm, 300 Hz pulses, making possible to generate electrons and hard x-ray pulses with duration less than 8 ps. The laser system, which generates the pulses that drive the x-ray diode and excite the sample, consists of a cw mode locked Nd:YLF laser, the master oscillator, a dye laser, a frequency mixing system and a ArF excimer laser used as a subpicosecond ,193 nm amplifier. This laser system is normally operated at 193 nm and a pulse width of 1.0 ps.

The x-ray diode consists of two flat electrodes - copper anode and aluminum photocathode - separated by 10 mm in vacuum of 10-9 Torr. The 193 nm, UV, radiation was directed onto the photocathode at 25o relative to the normal forming a spot with diameter of about 3 mm situated against the anode. The 1 ps electron pulse impinging onto the anode was broaden to 7.8 ps owing to space charge effects. The x-ray pulse duration is found to be the same as the electron pulse.

The x-ray radiation was measured with a large area, 16 bit, 2048 x2048 pixel chip, liquid nitrogen cooled x-ray CCD camera, designed specifically for direct x-ray imaging. The time width of the x-ray pulses was measured with a high repetition rate x-ray streak camera.

Using this system we performed time resolved x-ray diffraction experiments to study the lattice behavior during pulsed laser illumination by means of time resolved Bragg profile measurements. When part of the laser pulse energy is deposited in a material it generates a non uniform transient temperature distribution, carrier concentration or other effects, which alter the lattice structure of the crystal. The deformed crystal lattice will change the angle of diffraction for a monochromatic x-ray beam by DQ = - Dd/d cot , where d is the spacing of the diffracting planes, Dd is the change of the spacing due to an outside influence and   is the Bragg angle. The transient temperature and strain distribution in the crystal may be

studied by using thermal expansion coefficients and elastic constants of the crystal.

We have studied laser heating effect on three different crystals gold, platinum and gallium arsenide crystals by means of ultrafast time resolved x-ray diffraction. The time evolution of the lattice deformation and strain propagation can be extracted from time resolved Bragg profile. The experimental results matched well with the heat diffusion theory. The time resolved Bragg profile can be calculated with x-ray dynamical or kinematical theory depending on the property of the crystal : perfect or mosaic crystal. The transient temperature distribution can be monitored throughout the laser heating process. This data made it possible for us to determine the transient lattice deformation of crystals under pulsed 193 nm excitation. The lattice changes, and stress as a function of time and temperature have been determined for as a function of depth in the bulk and also as function of time and temperature.

We have also studied the x-ray diffraction pattern of liquids and liquid crystal by nanosecond and picosecond x-ray pulses. We shall describe the methods used and data obtained in our efforts to observe the structure of transients in the liquid state.

SINGLE MOLECULE FORCE SPECTROSCOPY
BY AFM

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Recent developments in piconewton instrumentation allow the manipulation of single molecules and measurements of inter-molecular as well as intramolecular forces. We took advantage of the high spatial resolution of the AFM and performed mechanical experiments with individual polymers and proteins. Dextran filaments anchored on a gold surface were picked up with the AFM tip and stretched[1]. The elongation of individual molecules was recorded as a function of the applied load. We found that at low forces the deformation of dextran is dominated by entropic forces and is well described by the Langevin function with a Kuhn length of 6Å. At elevated forces the dextran filaments show an additional segment elasticity of 650pN/Å which is attributed to the deformation of the bond angles. At a force of 300pN the dextran filaments undergo a massive conformational change and give by 0.6Å per ring. The high force conformation exhibited a segment elasticity of 1700pN/Å. The conformational change was found to be reversible and was corroborated by molecular force field calculations. In a similar fashion, Titin, a large muscle protein was investigated[2]. The elongation of individual native molecules was measured as a function of the applied load for different rates. A massive conformational change was found to occur at forces between 150 and 250pN. Measurements with several recombinant Titin Ig-segments of different length allowed us to identify this conformational change as the unfolding of individual Ig-domains. The refolding was found to be only partial and strongly rate dependent.

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Characterization of Liquid Crystalline Complexes Formed from Non-Mesogenic Anils with p-n-Alkoxybezoic Acids Induced by Hydrogen Bonding

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Hydrogen bonding interaction of N-(p-methoxy-o-hydroxybenzylidene)-p-aminopyridine (I) with a series of p-n-alkoxybenzoic acids results in the formation of liquid crystalline materials. The linear shape of these complexes is critical for the formation of liquid crystalline phases since the analogous complexes formed by the interaction of N-(p-methoxy-o-hydroxybenzylidene)-m-aminopyridine (II) with the same acids do not exhibit, in most of the cases, liquid crystalline behaviour. Detailed characterization studies were therefore performed for the complexes derived from the non-mesomorphic anil I with p-n-alkoxybenzoic acids employing DSC, optical microscopy and X-ray diffraction studies. Furthermore the range of existence of crystalline, liquid crystalline and isotropic phases will be shown in the phase diagrams of the binary mixtures of I with p-n-pentyloxybenzoic acid or p-n-dodecyloxybenzoic.

The results obtained can be summarized in the following: Hydrogen bonded 1:1 complexes form mesomorphic phases the nature of which depends on the length of the alkoxy chains. Specifically with alkoxy chains from methoxy to heptyloxy only nematic phases are formed while both nematic and smectic phases are obtained with octyloxy to dodecyloxy chains. Smectic phases are only formed for the complexes with tetradecyloxy- and hexadecyloxybenzoic acid.

Hydrogen bonding of the complexes was investigated with FT-IR at various temperatures covering crystalline, liquid crystalline and isotropic phases. Finally, molecular ordering was studied with X-rays as a function of temperature both in the crystalline and liquid crystalline phases.

Crystal Solving Procedures Applied to Peptides, Foldamers and Channel Forming Adamantyl /Peptide Hybrid Macrocycles

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Solving crystal structures by direct phase determination has become quite routine for many types of substances, providing that a sufficient number of X-ray reflections of reasonable magnitude can be measured. Resolution of 0.9 to 1.0 Å is usually desirable. Resolution of less than 1.15 to 1.2 Å causes severe problems for crystals composed of only C, H, N and O atoms. Problems arise for large molecules, molecules with flexible groups, crystals with several independent molecules per asymmetric unit, and structures with large channels or cavities containing water or disordered solvents. The above conditions contribute to an attenuation of the magnitude of the scattered reflections to the point that the number of reflections that can be used in phase determination is lessened and that the probability of the correctness of individual phases becomes small. At times, it is not the resolution that is the problem, but the fact that the intensities in general may be weak and also that any particular atom has a rather small contribution to a structure factor. Several examples of structure analyses of crystals that contain one or more of the above problems will be discussed.

Characteristics of five crystals are listed in Table 1. Routine direct phase determination as contained in the SHELXTL systems of programs[1], even for 10,000 trials in the TREF mode (tangent formula[2] refinement of phases), did not result in solutions for the crystals in Table 1. The crystal $MeO(Aib)_4$-$COPyrCO$-$(Aib)_4OMe$ (Py8Aib)[6] was solved in space group P1, rather than P$\bar{1}$. Reducing space group symmetry from, P$\bar{1}$, $P2_1$ or C2 to P1 (which doubles the number of unknowns) and later locating the symmetry element (a center of symmetry, a 2-fold screw axis or a 2-fold axis, for example) has been a successful methodology for many years.[3] In this particular case, fragments of two molecules (of the four molecules that needed to be placed in the cell) were recognized in the E-map[4] calculated from the best combined figure of merit in 1000 trials of TREF in the SHELXTL program.[1] Phases based on the 96 atoms in the fragments were refined and phases for additional reflections were determined by a partial structure procedure[5] (corresponding to TEXP in SHELXTL[1]). The E-map after one cycle of tangent expansion contained 242 of the 254 atoms in the structure. At this point a center of symmetry relating two of the molecules to the other two was recognized. The origin of the cell was translated to correspond to the center and the remainder of the structure was solved and refined in space group P$\bar{1}$.[6] Two procedural items should be noted. First, in the TREF calculation, the SUBS (subset) command had to be designated as type 8 (in which the reflections with the highest estimated α-values are used). Second, it is prudent, in cases where the fragments found in the initial E-map are relatively small, not to

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recycle in the TEXP procedure (3 cycles in the default instruction) but to examine the E-map after each single cycle and to select manually the atoms for the following cycle. Automatic selection of peaks by the program often results in too many incorrect "atoms" which lead to meaningless E-maps.

Three of the structures listed in Table 1 were solved by a vector search of a Patterson function followed by a translational search (the latter not required in space group P1) of a model from a known structure (or a fragment thereof) that corresponds closely to part of the unknown structure. The PATSEE program[7] is a free-standing program that is part of the SHELXTL package. The procedures for rotation, translation and tangent expansion are quite easy to use. The selection of the initial search fragment is problematical at times. For the cyclic(Val-Ser-Adm)$_2$ (where Adm is 1,3-dicarbonyl-adamantane) only 12 atoms, consisting of the adamantane frame plus two attached C atoms, could be used as the known model for the search fragment. Any additional atoms attached to this fragment would have introduced unknown rotational parameters. The 12-atom model, which represented only 10% of the unknown structure, yielded an additional 15 recognizable atoms after rotation and tangent expansion. The successful set of rotation parameters were ranked only fourth best with respect to the CFOM. In successive cycles of E-map and further tangent expansion, the number of atoms found increased to 38 and 93, after which difference maps were used. Two independent clam-shaped molecules form a channel that contains 9 water molecules. Almost all the carbonyl moieties and some of the NH moieties extend into the channel to form hydrogen bonds with the water.[6]

3

An entirely new type of helix has been constructed with β-peptides having the formula Boc-[NH⬡C(O)]$_n$-OMe. The structure of the tetramer (n=4) was solved routinely. The hexamer (n=6) had three molecules per asymmetric unit[8] and its solution by routine programs with exhaustive trials was not successful. A model consisting of 34 atoms from the tetramer (16% of the unknown atoms) was used more or less successfully for rotation and translation in the PATSEE program. The parameters for the second best fit, based on the CFOM according to criteria in the program, led to an E-map that showed a number of groupings of atoms that appeared to correspond to fragments of helical structures. None of the fragments in the E-map used individually would expand by means of the tangent formula to meaningful larger fragments. It was only after several fragments totaling 61 atoms were used together in the tangent expansion that some progress with growth on some of the fragments occurred. Repetition of the process showed very slow growth. Eventually, after the sites of 140 atoms were determined, the remainder of the 69 atoms were found by successive least-squares refinement and difference maps. The cause of the slow development of the structure is not apparent, especially since the ratio of the number of reflections observed $>4\sigma$ per atom was so much larger than in the usual experiment. It is true, however, that hydrophobic channels are formed which are filled with highly disordered $C_2H_4C\ell_2$ solvent molecules.

The next example concerns a conventional α-helix with many Phe residues, Boc-(VAFU)$_3$-OMe.[9] The intensity of scattering dropped to a low level at a relatively

small scattering angle and only 10% of the possible data were still barely measurable at a resolution of 0.9 Å. A model of 34 atoms from a known α-helix was used for the search fragment in PATSEE. The best ranked CFOM rotation parameters resulted in an E-map having a recognizable 31 atom fragment. Slowly, with manual intervention, the fragment was developed into two α-helices with the C^β atoms and some of the C^γ atoms. The six phenyl groups are still being eked out by alternate least squares refinement and difference maps. It is not clear at this time whether the space group is P1 with two similar independent molecules or C2 with one independent molecule. In each helix, the three phenyl groups are aligned along one side of the helix. The point of interest is the packing (perhaps interdigitation) of the phenyl groups in adjacent antiparallel helices.

The final structure analysis concerns the 16-residue antiamoebin (Ac-Phe-Aib-Aib-Aib-Iva-Gly-Leu-Aib-Aib-Hyp-Gln-Iva-Hyp-Aib-Pro-Phol).[10] The last half of the sequence is identical to that of zervamicin whose structure is known.[10] Further, both compounds crystallize in space group $P2_12_12_1$ with the a and b cell edges very similar in length and the c cell edge ~4.5 Å longer for the antiamoebin. It was suspected, correctly, that the conformation of the two molecules would be quite similar. The number of measured reflections was too meager for direct phase determination. The use of various size fragments taken from zervamicin as a search model was not successful in the PATSEE procedure. The initial placement of the antiamoebin molecules in the unit cell was accomplished by using Brunger's annealing least-squares program X-PLOR[12-14] on a model based on the zervamicin

molecule. Subsequently, alternate cycles of ordinary least-squares and difference maps corrected the gross misplacement of the phenyl ring in Phe[1] and located three cocrystallized octanol molecules. The particular interest in this structure is the assembly of an ion transport peptide in a membrane environment. The octanol may serve as a partial mimic for a lipid.

These different approaches for structure solution of large molecules with less than ideal X-ray data will be illustrated with actual examples and calculations.

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Table 1.   CRYSTAL CHARACTERISTICS

	Beta-Foldamer	Py8Aib	Cyclic (ValSerAdm)$_2$	Boc(VAFU)$_3$-OMe	antiamoebin/ 3 octanol
sp. gr.	$P2_1$	$P1^*$	P1	P1	$P2_12_12_1$
#indep. mols.	3	4	2	2	1
#C, N, O atoms	209	254	122	194	196
a, Å	15.393	16.064	12.604	8.838	9.142
b	21.764	16.156	12.623	19.878	28.590
c	27.869	21.655	16.575	23.369	44.289
α(deg)	90.	90.14	68.48	75.61	90.
β	101.46	101.38	89.87	89.95	90.
γ	90.	97.07	74.50	77.27	90.
V(g/cm^3)	9150	5465	2350	3872	11578
#indep. data	26600	14800	6316	11444	7438
				weak data	
#>4σ	13300	7250	3080	3347	4133
R_1 factor	11.7	(11.0)	8.8		11.9
Comments	grossly disordered solvent	disordered EtAc * actually in P$\bar{1}$	large water channel	6 wobbly phenyls *possibly in C2	2 disordered octanols
Structure Solution	Vector Search Rot/Trans 34 atoms from tetramer	TREF 1000 SUBS 8	Vector Search Rot/Trans on Adm+2C (12 atoms)	Vector Search 34 atoms from α-helix	Brunger annealing, tangent expansion

ESTEROLYTIC CATALYTIC ANTIBODIES - PRESENT FACTS AND FUTURE DREAMS [1]

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The concept of synthesizing stable analogs of the rate-limiting transition state for a given chemical reaction and using these as haptens to raise antibodies which could then serve as specific catalysts for thatreaction, has now been demonstrated for a considerable number of reactions[2]. Although this notion dates back to Pauling [3] and was first succinctly stated by Jencks [4], the field of catalytic antibodies took some time to become established. Today, it represents the most successful approach for achieving tailor-made catalysts and has been applied to some 100 different chemical reactions [5] with one catalytic antibody having very recently entered the marketplace as an Aldrich Chemical Co. reagent[6]; this antibody catalyzes aldol condensations and acts via a mechanism similar to that of Nature's aldolase enzymes [7].

Catalytic antibody research has both obvious practical aspects (programmed, "off-the-shelf" catalytic antibodies for applications in chemistry and biomedicine) and more basic ones, such as: understanding the mechanism of action of each of the novel catalysts so produced; uncovering the relation, if any, to natural enzymes; and answering questions concerning the evolution of efficient catalysts, the limits of catalytic parameters and properties using the antibody scaffold, and the possible extension of the information from, and experience with, catalytic antibodies to other tailor-made, enzyme-like catalytic systems.

Approximately half of the reported examples of antibody-catalyzed reactions involve ester-hydrolysis in which phosphonate haptens were used as the transition state analogs to elicit the antibodies. In addition, the recent X-ray structure analyses of a significant number of such anti-phosphonate esterolytic catalytic antibodies has afforded a wealth of information. These include the nature of the antibody-phosphonate interactions, and thereby conclusions as to the mechanism of reaction [8,9]; effects of pH on structural and mechanistic properties [10]; structural convergence of antibody active sites [11]; mechanisms of antibody inactivation [12]; detailed descriptions of reaction pathway, from substrate though transition state to product structures [13]; and elucidating the ways in which binding sites become catalytic sites [14].

Finally, each individual transition state analog which one designs and then synthesizes that successfully serves as a hapten to elicit catalytic antibodies generally gives rise to a number of different catalytic antibodies. Each of the resulting antibodies, which may differ slightly or even markedly from one another, are generally studied with regard to the substrate which is most congruent with the hapten used.

However, each of the antibodies may also be tested for reaction with substrates that vary in structure and one may then find unexpected, i.e., unprogrammed, reactivity patterns [15,16]. Especially when crystal structures are available, it may then be possible to draw new conclusions from the triangular relationship beween hapten-antibody-substrate and be able to predict new or optimal haptenic structures for a desired substrate. New data on the relationship of an achiral hapten, and the resulting chiral catalytic antibodies, with chiral substrates illustrates this notion.

A practical application of catalytic antibodies was illustrated above for chemical synthesis (aldol condensations) [6,7]. One of our goals is to extend the use of catalytic antibodies for therapeutic applications; this exciting possibility may allow us to tailor-make a specific detoxification catalyst in order to reverse a disease state. An illustrative example will be presented.

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Tetracycline-repressor acts as a molecular switch regulated by tetracycline binding.

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Tetracyclines are a class of molecules that have antibiotic action against bacteria by binding to their ribosomal 30 S subunit and inhibiting protein synthesis. Since the tetracyclines have been used and misused in the past 50 years, bacteria have developed resistance mechanisms of different types. These mechanisms are brought about by proteins encoded on moveable genetic elements like transposons or plasmids, which can be transmitted from one bacterium to the next so that a very efficient transfer of the genetic information occurs. The most common resistance mechanism in gram negative bacteria is due to a protein which is located in the bacterial membrane and exports tetracycline molecules as soon as they have entered the bacterial cell so that the tetracycline cannot reach the ribosomal 30 S subunits. The biosynthesis of this membrane protein (TetA) is regulated by tetracycline repressor (TetR) which binds to a specific DNA operator sequence located in front of the gene for the TetA molecule and also in front the gene for TetR. In the absence of tetracycline, the homodimeric TetR binds tightly to the operator by virtue of two helix-turn-helix motifs, which are a frequently observed supersecondary structural element interacting with the major groove of DNA. If, however, tetracycline enters the bacterial cell, it binds very tightly to TetR, induces a conformational change that widens the distance between the helix-turn-helix motifs in the TetR homodimer so that operator DNA is no longer tightly bound and released. This permits expression of the genetic information and production of TetA protein. It is inserted into the bacterial membrane and can now export tetracycline that has entered the cell, thereby preventing binding of tetracycline to the ribosomal 30 S subunit; the bacterium is now resistant against the antibiotic.

We have determined the crystal structures of TetR as such and in complexes with tetracyclines and with operator DNA. These studies show clearly how the antibiotic tetracycline is complexed with the TetR protein by a number of specific hydrogen bonds and

less specific hydrophobic interactions. The geometry of the binding site explains why some tetracyclines, which are chemically modified, bind with very different association constants. The binding of tetracycline to TetR induces a conformational change by unwinding one turn of an α-helix which in turn triggers a larger movement of the helix-turn-helix motifs so that DNA operator is no longer bond to TetR. We have also determined the crystal structure of TetR complexed with operator DNA which clearly suggests why this specific DNA sequence is recognized and tightly bound by the helix-turn-helix motif of TetR.

In summary, the crystal structures of uncomplexed and complexed TetR suggest the mechanism by which the antibiotic tetracycline acts as a switch in regulating the expression of the protein TetA. It elucidates how nature makes use of small conformational changes to trigger larger movements of parts of a protein molecule that are further away and have a very profound influence on the binding strength of TetR to operator DNA. This system shows that we can learn much in the field of supramolecular chemistry if we have deeper insight into functional mechanisms that are used by biological systems.

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INFLUENCE OF THE GUEST ON THE PACKING OF DIMERIC B-CYCLODEXTRIN COMPLEXES: ALIPHATIC MONO AND DIACIDS

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As a general idea, crystal engineering sounds as something unrealistic because it implies that all the interactions between the building blocks are known. However for certain classes of compounds, it is feasible to construct specific crystal packing at will. The dimeric complexes of β–cyclodextrin (βCD) is such a case.

βCD encloses a plethora of compounds to form inclusion complexes, the majority of which are dimeric. Those crystallise in four packing modes[1] two types of Channel Mode, a Chessboard Mode where the dimers are isolated and a form called Intermediate because it is intermediate between the Channel and Chessboard. The above modes of packing differ in the way that βCD dimers interact with each other in order to build the three-demensional lattice. Therefore, the influence of the guest on the topology of the surface of each dimeric complex is crucial.

Although it is difficult to postulate the crystal packing of a complex from the geometry and nature of a guest molecule alone, systematic studies have shown that in general (a) apolar guests form channel dimeric complexes where they are protected from the polar environment of the exterior of the dimer (b) guests bearing groups with H-bond forming ability influence towards isolation of the dimers and extensive hydration via H-bonding with surrounding water molecules and hydroxylic groups of neighboring dimers (c) as opposed to guests of intermediate tendency to be hydrated or with high tendency for self association that give an Intermediate packing in order to bring the dimers close.

The hypothesis is tested by a series of dimeric βCD complexes with aliphatic monocarboxylic and dicarboxylic acids. Diacarboxylic acids with 12-16 carbon atoms form complexes with a host:guest ratio 2:1 that crystallise in the Intermediate Mode. The carboxylic groups are linked by series of H-bonds via water molecules. Monocarboxylic acids (11-15 carbon atoms) forming complexes with a ratio host:guest 2:1 pack in the Channel Mode. The carboxylic groups isolated inside the hydrophobic channel form carboxylic dimers. On the contrary, monocarboxylic acids forming complexes of a ratio host:guest 1:1 with two carboxylic groups emerging from the primary faces of the βCD dimer, behave like dicarboxylic acids and pack in the Intermediate Mode[2]

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Design of Metallo-Cyclodextrins
# for Energy and Electron Transfer

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Biology provides many examples of light-sensitive macro- or supra-molecular intelligent systems that are capable of inducing directional motion of electrons and excitation energy. It is challenging to design systems that can perform similar functions to nature, not only for an enhanced understanding of the structural/spatial requirements for efficient energy and electron transfer but also for developing useful systems that can potentially convert light to chemical energy. From a synthetic point of view, it is not practicable to mimic the photosynthetic system but to use nature's construction paradigm instead, using a series of structural features organised via non-covalent interactions to achieve energy storage. This is our main incentive for designing "smart supramolecular systems" performing desired functions in contrast with other efforts where covalently linked systems are used.

Our approach involves employment of receptor molecules, cyclodextrins, to bring photoactive units together in close proximity. In this way we plan to control their spatial disposition without their requirement of covalent linkage. The interaction with light can then induce directional intramolecular energy or electron transfer depending on the nature of the species between two donor/acceptor (D/A) units as shown schematically.
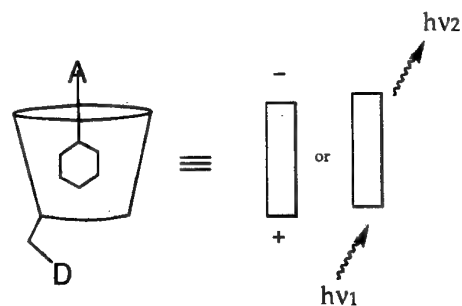
We have successfully synthesised modified cyclodextrins with appended tolyl-terpyridine units and studied the formation of metal complexes with Ru(II). The properties of the complexes will be presented and the potential of these metallo-receptors will be discussed.
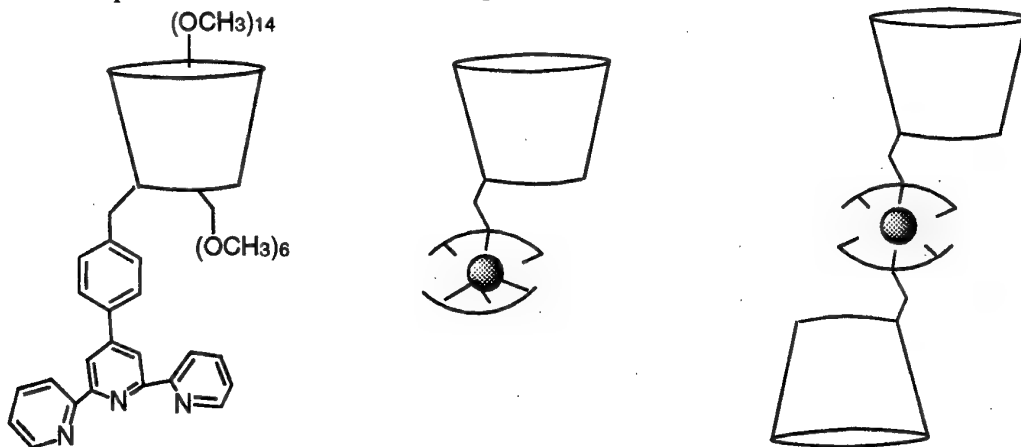
WEAK HYDROGEN BONDING IN CYCLODEXTRIN COMPLEX STABILISATION

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Cyclodextrins are macrocyclic host molecules composed of alpha(1-4)-linked D-glucoses. They readily form inclusion complexes with various molecules of suitable size. The molecular cavity is lined by C-H groups and by the O-4 atoms linking the glucose residues, rendering the cavity surface relatively hydrophobic in nature. If polar guest molecules are included in these cavities, they have limited opportunity to satisfy their hydrogen bond potentials.

Formerly, O/N-H..O hydrogen bonds with O-4 atoms and with hydroxyl groups at the cavity rims were regarded as the only possible host-guest hydrogen bonds in cyclodextrin inclusion complexes. However, we have found structural evidence for C-H..O hydrogen bonding [1-4] and also for directional C-H..pi interactions [2,4] in a number of cyclodextrin complexes (for background on weak hydrogen bonds, see Ref. [5]). In these hydrogen bonds, the C-H groups of the cavity wall can act as the donor and O-atoms or pi-systems of the guest molecules as the acceptor, but the situation can also be reverse with guest molecules donating C-H..O bonds to O-4 atoms of the cavity lining.

In quantum-chemical calculations, bond energies of ca. 1.0 kcal/mol were obtained for host-guest C-H..O interactions [6]. This is only a quarter or a fifth of energies of conventional O-H..O hydrogen bonds. The situation in general is interpreted as follows: if polar molecules are included in partly hydrophobic cavities, they form as many conventional hydrogen bonds as possible. The remaining hydrogen bond potential is then 'filled up' with weaker hydrogen bonds of the types C-H..O and X-H..pi. This leads to complex hydrogen bond networks involving interwoven conventional and non-conventional hydrogen bonds. The resulting situation can typically NOT be rationalised if the weaker hydrogen bonds are neglected.

This principle is not valid only for cyclodextrin cavities, but also helps to understand the arrangement of water clusters in internal cavities of proteins [7] and in interstitial cavities in peptide crystals [8].

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NANOCRYSTALS: BUILDING BLOCKS FOR NEW MATERIALS

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It is now well established that such fundamental properties as the melting temperature of a metal, the band gap of a semiconductor, or the remanence of a magnet, all depend strongly upon the size of the crystal, provided it is in the nanometer regime. As nanometer size crystals can now be made and observed routinely, this opens the prospect for creating materials with designed properties, not just by changing the chemical composition of the components, as has been done in the past, but by controlling the size.

The properties of nanocrystals change in systematic ways as a function of the size, slowly extrapolating to the familiar properties of extended solids. For most properties the size variation approximately follows a "scaling law." As the scaling laws are hypothesized and refined, it becomes possible to predict the properties of nanocrystals. As a concrete example, the optical properties of semiconductor nanocrystals vary systematically with size. The onset of absorption optical abosrption shifts to higher energy, and discrete structure develops in the spectra of ever smaller nanocrystals. A systematic effort is underway to understand further the actual evolution of structural, optical, electrical, and magnetic properties in nanocrystals.

In addition to the changes in physical properties which materials display when they are nanometer in scale, the chemical behavior is profoundly altered as well. First, it is important to realize that nanometer size crystals tend to spontaneously exclude defects and impurities, and melt at lower temperatures than the corresponding bulk solids. As a result, it is easier by far to make many small high quality crystals, than it is to make a single perfect one. In recent years chemists have developed general routes to the preparation of extremely high quality nanometer size inorganic crystals under conditions that are relatively simple (and hence inexpensive and scalable), when compared with techniques for the preparation of bulk or two dimensional materials. The final product consists of highly crystalline, monodisperse (5-10% variation in diameter), faceted nanocrystals, each coated with a monolayer of surfactant. For instance, CdS, CdSe, InP, InAs, Co, Ag, and Au nanocrystals are routinely prepared in this manner, with mean sizes varying between 1.5 and 20 nm diameter, and new preparations are under continuous development.

When an inorganic solid is comprised of only a few thousand atoms, it has a great deal of surface area. By binding an appropriate organic molecule to this inorganic surface, it is possible to make nanocrystals behave chemically just like an organic macromolecule. Typically an inorganic nanocrystal will be coated with a monolayer of surfactant, rendering the nanocrystals hydrophobic. In this configuration, the nanocrystals are soluble in non-polar solvents. If the solvent is removed, the nanocrystals aggregate but do not fuse, since they are separated by a layer of surfactant. These nanocrystals can be redissolved. Further, the surfactant can be exchanged off with another organic molecule, enabling the nanocrystals to be placed in almost any chemical environment. As a consequence of it, nanocrystals are really a new class of chemical reagent, and the inorganic components of materials can be organized using the well-developed principles and techniques of synthetic organic chemistry and molecular biology. The assembly of nanocrystals into well defined spatial arrangements is a topic of much current research.

Perspectives in Supramolecular Chemistry:
From Molecular Recognition towards Self-Organization

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Supramolecular chemistry has relied on more or less preorganised molecular receptors for effecting molecular recognition, catalysis and transport processes. A step beyond consists in the design of systems undergoing *molecular self-organisation*, i.e. systems capable of spontaneously generating a well-defined supramolecular architecture by *self-assembling* from their components in a given set of conditions.

The *molecular information* necessary for the process to take place must be stored in the components and acts through selective molecular interactions. Thus, these *programmed supramolecular systems* operate via molecular recognition.

Several approaches to self-assembling systems have been pursued concerning supramolecular assemblies of either organic or inorganic nature:

1) the generation of *mesophases* and *liquid crystalline polymers* of supramolecular nature from complementary components, amounting to macroscopic expression of molecular recognition;

2) the induction of molecular recognition directed processes in *supramolecular assemblies* and in *the solid state*;

3) the *self-assembly of inorganic species* based on ligand design and on the use of suitable coordination algorithms as expressed in - the formation of helical metal complexes, the *double-stranded and triple-stranded helicates*, - the spontaneous generation of *closed cage structures*, - the self-assembling of *inorganic grids* of metal ions based on suitably designed ligands.

Molecular information controlled, *"programmed"* and functional self-organising systems offer wide perspectives in supramolecular chemistry towards the design of functional supramolecular entities for network engineering, polymolecular patterning and nanotechnology.

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ABSTRACTS OF POSTERS

CONFORMATIONAL ASPECTS OF THE RECOGNITION BY BENZODIAZEPINE RECEPTORS OF THEIR LIGANDS

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The action of the 1,4-benzodiazepine derivatives on the nervous system on the molecular level has been mediated by their interaction with the membrane supramolecular receptor-ionophoric complex.

It includes the γ-aminobutyric acid receptors (GABA$_A$ Receptors), benzodiazepine receptors, chloric channel as well as binding sites of various exo- and endogenous biologically active substances.

It is known that there are tv kinds of the benzodiazepine receptors: with the high and low affinity. There is an opinion that their difference are determined by the different conformations that they have.

The efficiency of the 1,4-benzodiazepine transport to their target – benzodiazepine receptors is determined by their ability to form the reversible complexes with the blood albumin. In this case the complexation depends on the structure as well as on the preferential conformation of the 1,4-benzodiazepine ligand.

By the spectral methods and quantum-chemical calculations we have demonstrated that 1,2-dihidro-3H-1.4 benzodiazepine-2-ones in gas phase as well as solutions are in two unequivalent conformations: 1-st with the cisoidal conformation of amide group and 2-nd – with the anti-clinal conformation of amide group. These compounds in crystalline state have the pseudo-boat conformation deflecting from the ideal in degree that depends on the structure.

It has been shown that the 1,2-dihidro-3H-1.4-benzodiazepine-2-ones affinity for the benzodiazepine receptors increases with the increase of the 1-st conformer part. It has been determined that the affinity changes of these substances and the size changes of torsion angle N(1)RC(2)O are symbate.

IMPROVED STRUCTURE DETERMINATION OF COMPLEX SUPRAMOLECULAR FRAMEWORKS USING A CCD DIFRACTOMETER

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Since the installation of a Siemens SMART CCD Diffractometer 18 months ago we have collected and solved over 400 crystal structures including a large number of supramolecular framework compounds. A number of factors makes a CCD based instrument particularly suited to these studies. The ability to rapidly collect complete spheres of data on tiny crystals with large unit cells has been amply demonstrated. For many framework compounds suitably sized single crystals have been difficult to synthesize. For these cases it is desireable to use the diffractometer to rapidly screen many crystals. By discriminating against twinned and poor quality crystals it is possible to choose the best possible candidates for data collection.

I will give as an example the results of our studies of the low temperature ordering of a flexible guest-host framework compound. By combining NMR and single crystal X-ray diffraction we had previously been able to resolve details of a guest-induced distortion of the host framework in a toluene /t-butylcalix[4]arene complex. At low temperatures we had been able to detect evidence of a transient ordered phase. With the CCD diffractometer we have been able to collect a full low-temperature data set and resolve this ordering. More recently we have attempted to resolve a reported guest-induced distortion in a p-xylene adduct of Dianin's compound.

SECONDARY BONDS AND SUPRAMOLECULAR SELF-ASSEMBLY IN MAIN GROUP (ORGANO)METALLIC COMPOUNDS

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So far supramolecular chemistry basically concentrated upon hydrogen bonds, coordinative bonds and electrostatic interactions as driving force for supramolecular self-assembly, mostly inorganic and coordination compounds. Secondary bonds, also called closed shell interactions [characterized by interatomic distances intermediate between the sum of covalent atomic radii and van der Waals distances] were largely ignored. The poster will present results reporting secondary bond self-assembly of Main Group organometallics, through Tl...S, Sn...S, Pb...S, As...S, Sb...S, Bi...S and Te...S secondary bonds (semibonding interactions) leading to dimeric, trimeric or polymeric supramolecular aggregates.
The potential use of secondary bonds as intermolecular forces in supramolecular self-assembly will be stressed.

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An inexpensive approach to supramolecular architecture and its extension to solid-state arrays

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The control of the molecular architecture of a material is important because it provides a route to encoding the material's properties. Metallo-supramolecular chemistry has considerable potential as a method to achieve this goal, but is founded on ligand systems which require multi-step syntheses from expensive starting materials. This provides a barrier to wider access to and application of this field and to the rate at which novel molecular architectures are developed. We are addressing the challenge of developing new, inexpensive and easy-to-prepare systems.

Simply mixing inexpensive commercial reagents gives new ligands L in >90% yield. Reaction with copper(I) or silver(I) salts give dinuclear double-helical compounds. The beauty of these ligands lies in their ease of synthesis and inexpensive nature.
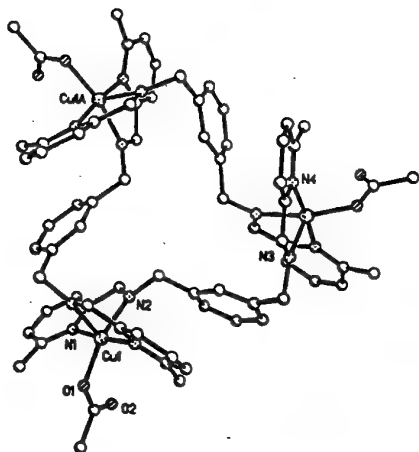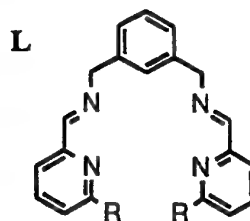
Using related ligands we have generate a range of architectures such as triple helices, grids and triangles.[1] We have also assembled molecular boxes by reacting simple polypyridines with suitable metal ions.[2] By adding binding sites to the outside the outside of our supramolecular structures we can control their assembly into polymeric arrays. Using our boxes we assemble infinite polymeric arrays containing precisely defined cavities.[3]
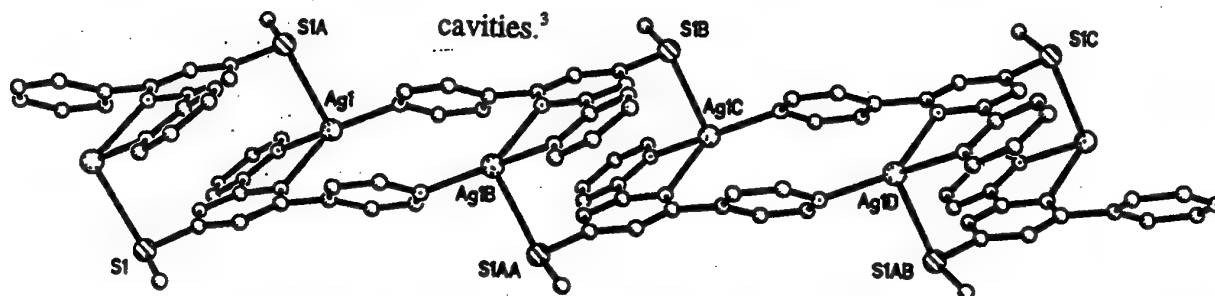
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SYNTHESIS AND CHARACTERIZATION OF TETRA 15-CROWN-5

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Unsubstituted phthalocyanines (Pc) which are not sensitive to heat, light, acids and bases resistant to oxidation are not soluble in common organic solvents. However, their solubility in organic solvents may be improved by attaching various substituent to the phthalocyanines molecules. Thus, their physical and chemical properties may also be altered.

In our previous works we synthesized phthalocyanines containing four 15-crown-5 moieties in which the crown ether parts are directly connected to benzenes of Pc (ref.1,2)

Instead of this rigid system in this study, 15-crown-5 unit was selected as an external part in order to enhance the complexation ability.

The generalizable synthesis of metal-free and metal (Ni, Zn) derivatives of a symmetrically tetrasubstituted phthalocyanine derived from 4-[(1,4,7,10,13-pentaoxa-2-cyclo-pentadecyl) metoxy]benzene-1,2-dicarbonitrile is described. The new compounds have been characterized by elemental analyses, IR, 1H and 13C NMR, UV-Visible, MS and TGA. Alkali ion-binding property of phthalocyanines containing crown ethers are receiving considerable attention in view of their effects on dimerization of the molecules (ref.3). In this work we could observed the high affinity of NiPc for the K+ ions in solvent extraction experiments. We observed the broadening of the Q-band transition at 680 nm in the electronic spectra.

The investigation about organization of the molecules (e.g. formation of ion channel) is under progres.

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STUDY BY ELECTROSPRAY MASS SPECTROMETRY OF LARGE DENDRITIC SUPRAMOLECULAR COMPLEXES

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The use of electrospray (ES) for the ionization of a very wide variety of biochemical and chemical compounds with low or high molecular masses is now well established in mass spectrometry (MS). Now, ESMS is also usually used in the field of supramolecular chemistry to characterize and to follow the formation of complexes and their intermediates in solution. [1 , 2]

In the case of some polynuclear transition metal complexes of dendritic nature, an unequivocal characterization is still missing, mainly due to stereogenic problems. Indeed, because of the numerous diastereoisomers in polynuclear compounds composed of polyazaaromatic Ru(II) complexes, the characterization by NMR is of limited use. For these artificial nanostructures, ESMS is the only analytical tool allowing their unambiguous characterization.

The aim of this work is the characterization by ESMS of a series of novel dendritic polymetallic complexes of Ruthenium (II). The largest complex with seven Rutheniums (II) has a molecular weight of 5602.2 Da. [3]

Three problems were encountered for the characterization by ESMS of this type of complexes :

1. The low amounts of sample available needed the use of a nanospray source. Then it was necessary to optimize the nanospray capillary for the use of organic solvents (acetonitrile, dichloromethane).

2. The low stabilitiy of these compounds in the gas phase made necessary the use of very mild ES interface conditions (low extraction cone voltage Vc and capillary exit voltage).

3. The partial decomposition of the counter-ions PF6- in the solution complicated the ES mass spectra since no clear series of multiply-charged ions could be detected.

For the four complexes studied, all the peaks observed in the ESmass spectra corresponded to the expected pure Ru(II) metallic complex. Ions were obtained by the loss of the counter-ions. For the monometallic, dimetallic and trimetallic complexes, the counter-ions were PF6- and the spectra were simple. The heptametallic complex was associated with different types of counter-ions resulting from the

hydrolysis of PF6- in solution. In this case, the ES mass spectrum was quite complex and high resolution analysis has been necessary for the ions identification. The stability of the complexes in the gas phase was shown as decreasing with the increase of their nuclearity.

ESMS brought clearcut evidences for the nuclearity of this series of Ru(II) dendritic complexes. Now, ESMS could be regarded as extremely valuable to prove the existence of very large polynuclear transition metal complexes, and paves the way to future design of artificial nanostructures with unambiguous characterization.

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SYNTHESIS, STRUCTURE, SELF-ASSEMBLY AND COMPLEXATION OF PHOSPHORUSCONTAINING CALIXARENES

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Calixarenes and resorcinarenes were functionalized by different organophosphorus groups at the upper or lower rim [1 – 7]. Conformation of the macrocyclic skeleton and properties of the compounds synthesised (including inherently chiral ones [3]) are strongly influenced by nature of these organophosphorus groups. X – Ray crystal and molecular structure of the family of phosphoruscontaining calixarenes and resorcinarenes as well as their host – guest complexes with different neutral organic molecules were investigated[1 – 6[. Self – assembly of some discussed compounds in solution, crystal state and Langmuir – Blodgett films were observed [5,7].

Complexation of these macrocycles in crystal state [5] (separation of benzene derivatives by extractive crystallisation method was achieved), in solution [6](stability constants of the complexes with organic guests and metal cations were determined, lithium selective ionophores were found), in LB – films [7](composite calixarene – polyaniline films were proposed for conductometric gas sensors) have been investigated.

Self – complexation phenomenon of the phosphoruscontaining calixarenes has been determined by X – ray and NMR methods [2,4,6].

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INTERCALATION OF MOLECULAR GUESTS INTO LAYERED VOXO$_4$ AND VOXO$_4$·yH$_2$O

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Intercalation reactions of tetragonal α_I - VOXO$_4$ and VOXO$_4$·yH$_2$O with molecular guests proceed as acid base processes between host layered lattice (Lewis acid) and donor atom of the guest molecule (base). The isolated corrugated sheet of the host is formed from the tetrahedra XO$_4$ linked to VO$_5$ square pyramids. The coordination number six is reached in the lattices of anhydrous VOXO$_4$ by the peak oxygen atom of the vanadium tetragonal pyramid from the adjacent layer. Layered complexes prepared by the reactions of the host and guest molecule are characterized by covalent bond of the donor atom of the guest to the vanadium atom in the host layer. A coordination polyhedron of the vanadium atom of the vanadyl group completes by this process to the distorted octahedron.

The penetration of the water molecules into the van der Waals zones of the anhydrous vanadyl phosphate and dehydration process of the dihydrate have been studied in details as a model intercalation and deintercalation reaction. Each tetragonal pyramid of VO$_5$ is completed by the water molecule in the deformed octahedron, further water molecule assume crystallographically nonspecified position between the (VOPO$_4$)$_\alpha$ layers creating the hydrogen bond V=O $\cdots$ H-O-H.

Intercalation of aliphatic alcohols with unbranched chains into the anhydrous VOSO$_4$ and VOPO$_4$ leads to the layered complexes of the composition VOPO$_4$·2C$_n$H$_{2n+1}$OH, where n=2-4, and VOPO$_4$·1.33 CH$_3$OH. By the reintercalation processes of the VOPO$_4$·2H$_2$O with alcohols C$_2$-C$_{18}$ in the microwave field the serie of the intercalates of the same composition has been prepared. It was found from the X-ray diffractograms, elemental analysis, from TG and DTA that in the fully intercalated product the alcohol molecules form a bilayer and their chains in *all-trans* configuration are arranged perpendicular to the layers. Diols C$_2$-C$_8$ are also in the perpendicular arrangement in the interlayer space but they form the monolayer. The ability of VOPO$_4$ to form mixed intercalates with the alcohols mixtures, and the dependence of alcohols content and interlayer distance of the intercalates formed on the composition of the starting mixtures of alcohols has been found. The kinetics of the intercalation of ethanol into anhydrous vanadyl phosphate has been studied by means of X-ray diffraction, thermomechanical analysis and a volumetric method.

Intercalates of the composition VOPO$_4$·2RNH$_2$ (R means aliphatic unbranched chain C$_1$-C$_{10}$) have been prepared and characterized by their basal spacing, DTA and IR spectra. The observed alternation of the basal spacing increments with the number of the carbon atoms of the chain indicates an oblique arrangement of these chains in the van der Waal's gap.

The complexes with aliphatic carboxylic acids (VOXO$_4$·RCOOH, X = S, P, As; R=C$_1$-C$_4$) are formed either by the intercalation reaction of the anhydrous host lattice with liquid acid or by reintercalation reactions of the VOXO$_4$·yH$_2$O or by reintercalation of the intercalates VOXO$_4$·2C$_2$H$_5$OH with the acid in the presence of a dehydrating agent. The even - odd alternation of the basal spacing increments can be explained by an oblique arrangement of the chains.

Glycine intercalated vanadyl phosphate (VOPO$_4$·NH$_2$CH$_2$COOH) retains layered structure of the parent phosphate with the basal spacing corresponding to the perpendicular arrangement of the glycine chains in the interlayer space. IR spectra confirm presence of glycine molecules in the intercalate as zwitterionic species.

ALPHA CYCLODEXTRIN DIMERIC COMPLEXES WITH 1,12-DIAMINODODECANE AND 12-AMINODODECANOIC ACID

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The structures of the alpha cyclodextrin (αCD) dimeric complexes with 1,12-diaminododecane (ADA) and 12-aminododecanoic acid (ADO) have been determined.

ADA is crystallized in $P2_1$, a=14.10(2), b=16.90(2), c=24.45(3)Å, β=97.40(3)°. The αCD molecules form dimers alligned along the *b* axis in a way resembling the Intermediate packing mode of βCD complex molecules [1]. One diamine molecule, very well localized, spans the cavity of each αCD dimer along its axis. The nitrogen atoms protrude from the primary hydroxyl side and are directly hydrogen bonded to primary hydroxyl oxygen atoms of consecutive dimers.

ADO is crystallized in $P2_12_12_1$, a=14.07(1), b=27.44(2), c=31.20(2)Å. The αCD molecules form dimers that include one molecule of the guest very well localized. The aminoacid molecule is extended parallel to the dimer axis, its carboxylic group located at the level of one primary hydroxyl side while the amino group is slightly protruding from the other. The carboxylic and the amino groups of the guest molecule are involved in several hydrogen bonds with primary hydroxyl oxygen atoms of the same and neighboring cyclodextrin molecules as well as with water molecules.

Alpha cyclodextrin dimeric complexes crystallize mostly in P1 the dimers forming endless channels parallel to crystallographic *c* axis. [2,3] The disruption of the channels occurred in the title complexes is attributed to the lengthy aliphatic guest molecules extending to both primary faces of the dimer. Thus, by having a guest possessing hydrogen bonding ability at their surfaces the dimers' interaction scheme is differentiated.

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A SPHERICAL SUPRAMOLECULAR HOST THAT POSSESSES A VAST CAVITY.

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Self-assembly processes which lead to hollow nano-sized spherical arrays are common in Nature (*e.g.* spherical viruses, fullerenes). A common feature of these shell-like architectures is their ability to encapsulate guests whose size, shape, and chemical exteriors complement their inner surfaces. Such properties have undoubtedly inspired the recent emergence of monomolecular and supramolecular dimeric molecular capsules (*e.g.* carcerands, cryptophanes). Despite the synthesis of these *pseudo*-spherical capsules, however, structural mimicry of frameworks akin to viruses and fullerenes has remained elusive. Here we present the first example of such a system: a nano-sized spherical host held together by 60 hydrogen bonds. We demonstrate the ability of this host to maintain its structure in solution and encapsulate guest species within a vast cavity that possesses an interval volume of 1375 E^3. General design principles anticipated to lead to the construction of similar hosts are also presented.

SELF – ASSEMBLY OF LAYERED METALLO-ORGANIC CLAY MIMICS

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This poster reports the self-assembly of the complexes, Ag(1)X, where 1 is the ligand, 2, 11-dithia-[5](1,2)[5](4,5)-cyclophane, and X represents a range of anions. 1 incorporates a rigid durene unit to preclude chelation to a single metal center. The complexes form an infinite array composed of cationic Ag(1) layers and interlamellar anions as determined by both single crystal and powder X-ray diffraction. This is structurally analogous to an anionic clay. The complex, Ag (1)BF4 may be wetted with a range of solvents to "swell" the interlayer region. Layer spacings, as determined by powder X-ray diffraction, range from 9.34 (1) E for toluene to 15.09 (1) E for dimethylformamide, c.f. 8.45 (1) E for dry Ag(1)BF4. The exchangeability of interlamellar anions is also demonstrated. DSC revealed that the structures were generally stable to well over 100 °C.

Ag(I)-Assisted MALDI-TOF Mass Spectrometry as a Novel and General Characterization Technique for Neutral Hydrogen Bonded Assemblies.

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The chemistry of the *non-covalent* bond has developed into an area of enormous interest to a wide variety of scientific and technological disciplines, ranging from materials science to molecular electronics. The characterization of non-covalent assemblies is far from being straightforward. Particularly the exact molecular weight determinations are still a matter of very limited success and currently remain one of the major challenges in the field. Most characterization studies primarily rely on NMR data[1] often in combination with VPO and/or GPC data,[2] techniques that give average molecular weight values with an error up to 20%. Occasionally light-scattering data[3] or single X-ray crystal structures are reported.[4] Ion-Labeling Electron Spray Mass Spectrometry techniques were reported by Lehn[5] and Whitesides[6] for the characterization of hydrogen-bonded assemblies, but their methods have only been successful for one particular type of aggregate.

In this paper we report a novel and general method for the exact molecular weight determination of neutral non-covalent aggregates, based on MALDI-TOF mass spectrometry in combination with a silver labelling technique. The method relies on the ability of the soft Ag^+ cation to coordinate to a variety of different Lewis basic functionalities, e.g. cyano, acetylenic, as well as electron-rich aromatic rings, thus creating a positively charged complex that can be easily detected by MALDI-TOF. In this paper we describe our first MALDI-TOF results on a class of neutral hydrogen-bonded assemblies, for which mass spectrometric molecular weight determinations have sofar not been successful.

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Preparation of an amino acid derivative of β-cyclodextrin and it use for the complexation of dioxaspiroundecane

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Grafting of amino acid derivatives on cyclodextrins has been achieved frequently [1-3]. Peptides have also been introduced on cyclodextrins [4]. We present a simple access to amino acids and some of their derivatives containing a cyclodextrin moetie in the side chain and their use for the complexation of dioxaspiroundecane (pheromone of the olive fruit fly).

The synthesis of these compounds relies in the first step on the acylation of monoaminomonodeoxy-β-cyclodextrin (6^I-amino-6^I-deoxycyclomaltoheptaose) with partially protected derivative of glutamic or aspartic acids followed by the removal of the protecting groups.

1a : n = 1; 1b : n = 2
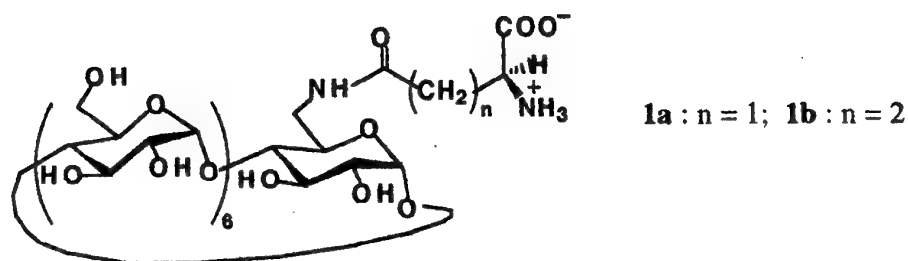
These compounds are extremly soluble in water(> 150 %). The inclusion complexes was prepared by addition of 1.2 equivalent of the pheromone to a stirred solution of the amino acid derivatives **1a-b**. As expected, the solubilities of the inclusion complexes (10 % w/v) are lower than the solubility of **1a-b**. However the solubility of the pheromone in water is at least 1000 times greater than in the case of complexes with β–CD.

A derivative of **1b** protected on the nitrogen by a *tertt*-butyloxycarbonyl group (BOC) have been prepared. This compound is suitable to be incorporated in peptides.

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Supramolecular Assemblies of β-Cyclodextrin with Pyrene, Alcohols and Water

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Much of the interest in cyclodextrin complexes hinges on the fact that the water soluble, torus-shaped cyclodextrins have an apolar cavity that binds and solubilizes guests with low solubility in water. A commonly accepted model for complex formation suggests that the complex forms when a suitable hydrophobic molecule displaces water from the cavity.

Guests that have been solubilized in aqueous solution as cyclodextrin complexes include many polynuclear aromatics. The archytypical complex of a polynuclear aromatic with β-cyclodextrin is that of pyrene. Many models have been presented for the geometry of the complex. Invariably, these involve insertion of pyrene into the apolar cavity, and construction of a model shows that about half of the pyrene protrudes. A second cyclodextrin then can enclose the protruding portion thus giving a 2:1 clamshell-like complex. The plausibility of such ideas has been confirmed by modelling calculations.

We have examined single crystals of the ternary complexes with n-octanol and cyclohexanol as co-guests by X-ray diffraction and found that in both cases pyrene is sandwiched between two cyclodextrins forming a head-to head dimer. The alcohol guests penetrate the cyclodextrins from the primary hydroxyl side, thus "stoppering" the open ends of the dimer. Close examination of the pyrene site shows that the guest lies in the broadest part of the dimer cavity with the positions of the host molecules unpertubed by the presence of the guest. The only interaction between guest and host appears to be the van der Waals contacts between pyrene H atoms and cyclodextrin hydroxyls. This illustrates that the space enclosed by a complete network of hydrogen-bonded water molecules and hydroxyl groups also can be considered as a hydrophobic site, a situation reminiscent of the cages formed by water molecules occupied by small hydrophobic molecules within in the clathrate hydrate lattices.

The common pattern for the two structures presented is that each guest, pyrene and the alcohol, interact with the host in a non-competitive way. There seems to be no particular reason why other polyaromatics should not occupy the same site as pyrene, or why the third component must be an alcohol.

NOVEL PEPTIDE NANOSTRUCTURES THROUGH SELF-ASSEMBLY

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The development of novel materials and molecular devices in the nanometer scale is an active area of research. In this presentation, we will report our appoach to the preparation of structurally-define nanostructures. The strategy involves the synthesis of crown ether modified peptides for their use as molecular frameworks for the formation of self-assembled rotaxanes with polyammonium guests. We will describe the synthesis and the characterization of the first prototypes, as well as the potential of this novel strategy.

Oriented Crystalline Thin Films of Tetracosanedioic Acid and its Metal Salts at the Air-Aqueous Solution Interface

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The crystalline packing arangement of monolayer and multilayer films, formed by the self-assembly of amphiphilic, non amphiphilic and bolaamphiphilic molecules at the air-water interface, has been determined, in-situ, with almost atomic resolution by means of synchrotron grazing incidence X-ray diffraction (GIXD). In these films, at low surface pressure, the long molecular axis is aligned either normal to the water surface or tilted by an angle of maximally 40° from the normal. The changes from tilted molecular chain axes to vertically aligned molecules in the packing arrangement of long-chain carboxylic acids monolayers, as induced by the presence in the subphase of Cd2+, Ca2+, Pb2+ ions have been also determined by GIXD.[1]

Here we report on the self-assembly process of the bolaamphiphile a,ω-tetracosanedioic acid, $HOOC-(CH_2)_{22}-COOH$, that undergoes a dramatic change in molecular orientation when the subphase is changed from pure water to an aqueous subphases containing Cd2+ and Pb2+ ions. These metal ions bind to both carboxylate ends of the molecule and force the long hydrocarbon chain to lie parallel to the water surface. Once formed, the salt molecules self-assemble into oriented crystalline thin films, about 50Å thick, but with the chains and the bound ions perfectly ordered laterally over distances up to 1000Å.

GIXD and specular X-ray reflectivity measurements demonstrate that in these multilayer crystallites the molecular chain axes are oriented parallel to the surface and the metal ions form layers oriented perpendicular to the surface. The oriented crystallites preserve their integrity after transfer from the liquid surface onto freshly cleaved mica support, as imaged by scanning force microscopy, and have been used in the preparation of quantum dots.

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THE CRYSTAL STRUCTURE OF THE INCLUSION COMPOUNDS OF TWO PLANT GROWTH REGULATORS IN β-CYCLODEXTRINS

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In a systematic study of inclusion compounds of plant growth regulators, the complexes of the β-napthoxyacetic acid and the trans-cinnamic acid in β-Cyclodextrin have been prepared. The former is an auxin while the latter an inhibitor and both crystallize in the monoclinic space group C2 with cell dimensions respectively a=19.341, b=24.632, c=15.975 Å and α=108.77° and a=19.422, b=24.461, c=15.941 Å and α=108.648°. The refinement is in progerss and the R value for both structures has reached 12.5. Preliminary tissue culture tests have proved that the complexation of β-napthoxyacetic acid with β-CD enhances the biological activity of the plant tissues tested. This has been indicated by the results concerning the electrical activity of the plant tissues.

AQUEOUS NMR STUDY OF THE INCLUSION COMPLEXES OF LINEAR ALIPHATIC α, AMINOACIDS WITH α-CYCLODEXTRIN

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α,ω-Aminoacids constitute a class of compounds which can readily condense to polyamides, under conditions of solid state polymerization. Wenz and coworkers have shown[1] that the inclusion complex of 11-aminoundecanoic acid with α-cyclodextrin (αCD) can undergo polycondensation to afford a polyamide bearing about 20 αCD rings. In our effort to extend our studies of αCD and βCD inclusion complexes with long aliphatic acids[2] to diacids[3] and aminoacids,[4] we have studied in detail the inclusion behaviour of 11-aminoundecanoic acid and 12-aminododecanoic acid in aqueous solution, in the presence of αCD by NMR spectroscopy.

11-Aminoundecanoic acid (11AMO) and 12-aminododecanoic acid (12AMO) form 2:1 *and* 1:1 inclusion complexes with αCD. The complexes were examined by NMR at pH 7.3 and 13.6 using the mole ratio and the continuous variation methods. It was found, that in both pHs there exist mixtures of binary and ternary complexes (one and two αCD molecules per aminoacid). At higher pH the 1:1 complexes exist at concentrations higher than those at neutral pH. This could be due to increased electrostatic repulsions in the 2:1 complexes between the carboxylate anions of the guest and the hydroxyl groups of αCD.[5] On the other hand, 12AMO, even though it is only a methylene unit longer than 11AMO, tends to form complexes enriched in the 2:1 constituent at both pHs. The equilibrium between the two complexes is evident as the aminoacid ^{1}H and ^{13}C signals are exchange broadened, their shape and intensity being dependent upon the molar ratio of host and guest. Finally, the complexes either in the 1:1 or the 2:1 form, give 2D ROESY spectra consistent with structures having the aminoacids extend through the one or two rings of αCD, and not folded, with the polar ends outside.[6]

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